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FRI0281

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS WITH STABLE ANKYLOSING SPONDYLITIS RECEIVING TUMOR NECROSIS FACTOR INHIBITOR: CONTINUED VS WITHDRAWN

O. C. Kwon¹, J. H. Park¹, M. C. Park¹. ¹Yonsei University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)

Background: A recent recommendation from the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (ACR/SAA/SPARTAN) suggests withdrawing non-steroidal anti-inflammatory drugs (NSAIDs) in patients with stable ankylosing spondylitis (AS) receiving tumor necrosis factor inhibitor (TNFi) and NSAIDs.¹ However, the level of evidence for this statement is very low with lack of evidence supporting this recommendation. No studies have directly compared stable AS patients receiving TNFi with NSAIDs, and those receiving TNFi without NSAIDs.

Objectives: To compare the disease activity in stable AS patients receiving TNFi, according to the use of NSAIDs.

Methods: In total, 189 patients with stable AS receiving TNFi were included. Patients were classified into NSAID withdrawn group (n=48) and NSAID continued group (n=141), according to the use of NSAIDs. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured every 3 months, and Bath ankylosing spondylitis disease activity index (BASDAI) was measured every 6 months as parameters to evaluate disease activity. ESR, CRP, and BASDAI at each time point, and time-averaged values of each parameter during the observation period of one-year were compared between the two groups. Repeated-measure ANOVA was performed to compare changes in disease activity parameters during the observation period between the two groups.

Table. Disease activity measures during observation period

	NSAID withdrawn (N = 48)	NSAID continued (N = 141)	P value
At 3 months			
ESR (mm/hr), median (IQR)	5.0 (2.0–14.0)	7.0 (2.0–15.0)	0.712
CRP (mg/L), median (IQR)	0.5 (0.2–1.5)	0.8 (0.3–1.8)	0.613
At 6 months			
ESR (mm/hr), median (IQR)	5.0 (2.0–15.0)	7.0 (2.0–15.0)	0.278
CRP (mg/L), median (IQR)	0.6 (0.3–1.8)	0.8 (0.3–2.1)	0.335
BASDAI, mean ± SD	2.019 ± 0.569	2.226 ± 1.028	0.187
At 9 months			
ESR (mm/hr), median (IQR)	4.5 (2.0–13.8)	7.0 (2.8–17.0)	0.261
CRP (mg/L), median (IQR)	0.5 (0.3–1.6)	0.8 (0.3–2.2)	0.129
At 12 months			
ESR (mm/hr), median (IQR)	6.0 (2.0–13.0)	9.0 (3.0–19.0)	0.050
CRP (mg/L), median (IQR)	0.6 (0.3–2.1)	1.0 (0.4–3.1)	0.151
BASDAI, mean ± SD	2.168 ± 1.066	2.197 ± 1.002	0.867
Time-averaged values			
ESR (mm/hr), median (IQR)	5.3 (2.6–15.2)	8.4 (3.8–14.7)	0.096
CRP (mg/L), median (IQR)	0.8 (0.4–1.8)	1.1 (0.5–2.9)	0.136
BASDAI, mean ± SD	2.137 ± 0.557	2.227 ± 0.706	0.421

Abbreviations: NSAIDs, non-steroidal anti-inflammatory drugs; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath ankylosing spondylitis disease activity index.

Results: The level of ESR, CRP, and BASDAI at baseline and during the observation period did not differ between the two groups. The time-averaged values of ESR (p=0.096), CRP (p=0.136), and BASDAI (p=0.421), and changes of ESR (p=0.101), CRP (p=0.714), and BASDAI (p=0.613) during the observation period were not significantly different between the two groups.

Conclusion: The continued use of NSAIDs in patients with stable AS receiving TNFi had no additional benefit in controlling the disease activity, as compared to patients who withdrew NSAIDs. Considering the risk of toxicity of long-term NSAID use, withdrawal of NSAIDs in stable AS patients receiving TNFi may be preferable.

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FRI0282

CONVENTIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS THERAPY HAS NO EFFICACY IN SLOWING SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS: RESULTS FROM 18-YEAR LONGITUDINAL DATA

T. H. Lee¹, B. S. Koo², S. Lee³, Y. K. Lee¹, J. S. Oh⁴, S. Y. Park⁵, T. H. Kim¹.

¹Hanyang University Hospital for Rheumatic Diseases, Department of Rheumatology, Seoul, Korea, Rep. of (South Korea); ²Inje University Seoul Paik Hospital, Inje University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea); ³Hanyang University Hospital, Department of Radiology, Seoul, Korea, Rep. of (South Korea); ⁴Asan Medical Center, University of Ulsan College of Medicine, Department of Biomedical informatics, Seoul, Korea, Rep. of (South Korea); ⁵Asan Medical Center, University of Ulsan College of Medicine, Department of Clinical Epidemiology and Biostatistics, Seoul, Korea, Rep. of (South Korea)

Background: In the treatment of ankylosing spondylitis (AS), conventional disease-modifying antirheumatic drugs (cDMARDs) are generally recommended only in patients with peripheral arthritis. However in daily clinical practice, sulfasalazine (SSZ) and methotrexate (MTX) have still been considered on the basis of their anti-inflammatory effect when non-steroidal anti-inflammatory drugs (NSAIDs) are not available and when it is difficult to start tumor necrosis factor (TNF) inhibitors. Nonetheless there is few data about the impact of the cDMARDs on the prognosis of spinal progression.

Objectives: The aim of this study was to investigate the effectiveness of SSZ and MTX on the spinal radiographic progression in patients with AS.

Table 1. Association of clinical covariates and DMARD intervals with the rate of mSASSS change

Variable	Multivariate analysis			
	Model 1		Model 2	
	β (95% CI)	p	β (95% CI)	p
On-DMARD intervals	-0.081 (-0.276 to 0.115)	0.418		
On-SSZ intervals			-0.001 (-0.211 to 0.189)	0.913
On-MTX intervals			-0.180 (-0.439 to 0.078)	0.172
Sex (female)	-0.449 (-0.782 to -0.117)	0.008	-0.440 (-0.775 to -0.105)	0.010
Age	0.012 (-0.001 to 0.026)	0.061	0.012 (-0.001 to 0.025)	0.076
Eye involvement	0.572 (0.264 to 0.880)	< 0.001	0.577 (0.268 to 0.886)	< 0.001
Peripheral joint involvement	-0.508 (-0.810 to -0.206)	0.001	-0.513 (-0.817 to -0.210)	0.001
HLA-B27 positivity	†		†	
NSAIDs	†		†	
Glucocorticoids	†		†	
ESR (log)	0.176 (0.087 to 0.265)	< 0.001	0.178 (0.088 to 0.268)	< 0.001
BASDAI (square root)	†		†	

†Not included in the model because the value did not show potentially significant association in univariate analysis (p > 0.1).

Methods: A total of 301 patients who have been treated with cDMARDs were enrolled from 1,280 patients in a single center cohort during 18 years of follow up. For each patient, time intervals of periods were created according to the prescription records. 'On-DMARD' intervals were time intervals of periods with SSZ or MTX treatment and 'off-DMARD' intervals were time intervals of periods without both SSZ and MTX treatment. The intervals were the periods excluding the treatment periods of TNF inhibitors. Radiographic progression was evaluated by the rate of Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) change, an increase or decrease of mSASSS change per year. A generalized estimating equation models with adjustment for confounding covariates were used to evaluate the efficacy of cDMARDs on the radiographic progression.

Results: The number of 732 on-DMARD intervals and 1,027 off-DMARD intervals were obtained. Among the on-DMARD intervals, the proportion of intervals treated with SSZ (on-SSZ intervals), MTX (on-MTX intervals) and both of them (on-SSZ/MTX intervals) were 96.2%, 19.9% and 16.1%, respectively. In the multivariable regression analysis, there was no significant decrease in the rate of mSASSS change during cDMARDs therapy (β = -0.081, p = 0.418) (Table 1). And the mean rate of mSASSS change were 0.61 during on-DMARD intervals and 0.69 during off-DMARD intervals after adjustment of other covariates.

Conclusion: Treatment with cDMARDs in AS did not show significant impact in retarding spinal progression. In patients with AS, treatment with biologics rather than cDMARDs may be more effective in slowing radiographic progression.

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FRI0283

CO-MEDICATION WITH CSDMARD HAS LITTLE EFFECT ON THE RETENTION OF TNF INHIBITORS IN PSORIATIC ARTHRITIS, RESULTS FROM THE EUROSPA COLLABORATION

U. Lindström¹, D. Di Giuseppe¹, B. Delcoigne¹, B. Glintborg¹, B. Moeller¹, M. Pombo-Suarez¹, C. Sánchez-Piedra¹, K. Eklund¹, H. Relas¹, B. Gudbjornsson¹, T. Love¹, G. T. Jones¹, A. Ciurea¹, C. Codreanu¹, R. Ionescu¹, L. Nekvindova¹, J. Zavada¹, N. Atas¹, S. Yolbaş¹, K. Fagerli¹, B. Michelsen¹, Z. Rotar¹, M. Tomsic¹, F. Iannone¹, M. J. Santos¹, P. Ávila-Ribeiro¹, L. Midtbøll Ørnbjerg¹, M. Østergaard¹, L. T. H. Jacobsson¹, J. Askling¹, M. Nissen¹. ¹EuroSpA Research Collaboration, On behalf of the DANBIO (Denmark), ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorix.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Romania), ARC (Netherlands), BSRBR-AS (United Kingdom), GISEA (Italy), Copenhagen, Denmark

Background: Previous studies have suggested similar effectiveness, but longer treatment retention, for tumor necrosis factor inhibitors (TNFi), when used in combination with a conventional synthetic disease modifying anti-rheumatic drug (csDMARD) in psoriatic arthritis (PsA).

Objectives: To describe patients with PsA initiating a first TNFi as monotherapy compared to combination therapy, and to explore 1-year treatment retention of TNFi in the two groups.

Methods: Patients with PsA starting a first TNFi (2006-2017) were identified in biologics registers of 13 European countries, and data were pooled for analysis. Co-medication with csDMARD was determined at TNFi start.

Because of large inter-country variation in TNFi retention, countries were split into two strata, depending on each country's 1-year retention rate for TNFi being above (stratum A) or below (stratum B) the average 1-year retention rate.

TNFi treatment retention was compared through Kaplan-Meier curves; the proportion remaining on the TNFi at one year; and hazard ratios (HR) during the first year: (i) crude; adjusted for (ii) country-strata, and (iii) country-strata, sex, age, calendar year, DAS28 and disease duration. In model (iii) only registers contributing >1000 patients or <33% missing data for DAS28 were included.

Results: A total of 14778 patients with PsA starting a first TNFi were included. Baseline disease activity was similar within stratum B, but higher for the combination treatment group in stratum A (table 1).

Table 1. Baseline characteristics

Country strata	Stratum A		Stratum B	
	TNFi monotherapy N=2120	TNFi/csDMARD combination N=2128	TNFi monotherapy N=3369	TNFi/csDMARD combination N=7161
Females	52%	51%	53%	51%
Age, years	49.7 (12.2)	48.7 (11.8)	48.8 (13.0)	48.9 (12.2)
Disease duration, yrs	6.4 (7.0)	6.8 (6.8)	5.9 (7.5)	5.9 (7.1)
Tender joints 28	5.5 (6.3)	8.0 (6.3)	5.6 (6.0)	5.6 (5.7)
Swollen joints 28	2.8 (4.3)	5.6 (5.0)	3.0 (3.8)	3.3 (3.8)
VAS pain	54 (29)	62 (24)	59 (23)	56 (24)
DAPSA-28	24.6 (18.6)	36.2 (17.6)	27.3 (15.6)	27.2 (15.2)
DAS28 (CRP)	3.5 (1.4)	4.7 (1.3)	4.0 (1.2)	4.0 (1.1)
Concomitant csDMARD				
Methotrexate	-	76%	-	79%
Sulfasalazine	-	15%	-	15%
Other csDMARD	-	49%	-	25%

Numbers are means (sd) unless otherwise stated.

The Kaplan-Meier curves for the treatment groups were similar within each stratum (fig 1), as were the proportions remaining on TNFi after one year, stratum A: monotherapy 86% (95%CI: 85-88) vs. combination 86% (84-87), stratum B: 71% (69-72) vs. 73% (72-74). The HRs for TNFi discontinuation (ref=TNFi monotherapy) were: (i) 1.06 (0.98-1.13), (ii) 0.94 (0.87-1.01), (iii) 0.89 (0.83-0.96), including 13078 patients (9 countries) for model (iii).

Conclusion: In this exploratory study no benefit in TNFi retention was observed for csDMARD combination therapy in crude analyses, while in adjusted analyses an 11% lower risk of TNFi discontinuation was found. These preliminary results offer limited support for use of combination therapy in PsA. Further analyses will

explore to what extent the results are affected by inter-country heterogeneity and differences between TNFi.

Figure 1. Retention rate of TNFi monotherapy vs. TNFi and csDMARD co-medication in psoriatic arthritis, stratified by each country's one-year retention rate being above (stratum A) or below (stratum B) the average one-year retention rate.

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