Pilot study: non-steroidal anti-inflammatory drugs attenuate active inflammatory sacroiliac joint lesions in patients with early axial spondyloarthritis

Sirs,

Treatment of axial spondyloarthritis (axSpA) aims to attenuate inflammatory arthralgia, prevent and delay fusion of axial joints, and maintain range of motion (1). Non-steroidal anti-inflammatory drugs (NSAIDs) are the first choice of treatment in axSpA, and TNF-α inhibitors can be used in patients with intolerance or contraindication to NSAID (1). TNF-α inhibitors have been widely studied and treatment guideline from the Assessment of SpondyloArthritis international Society (ASAS) – European League Aginst Rheumatism (EULAR) recommend tapering a TNF-α inhibitor if the disease activity is stabilized (1). However, initial optimal dose and duration of NSAID for axSpA patients are not yet established.

Baseline fat metaplasia in the sacroiliac joint (SIJ) has been associated with spinal structural deterioration (2), and another study revealed an association between structural damage in the SIJ and spinal mobility in axSpA (3). Fat metaplasia is a chronic lesion in the SIJ that can evolve from bone marrow oedema (BMO) (4). Therefore, preventing fat metaplasia and resolving BMO can attenuate deterioration of structural damage and spinal mobility in axSpA.

The present study aimed to determine the therapeutic effect of NSAIDs on active inflammatory lesions (BMO) in the SIJ in early axSpA. Additionally, the results could be used to recommend initial optimal dose and duration of NSAID in axSpA patients. Additionally, correlations between clinical/biochemical parameters and MRI finding were assessed.

We enrolled patients with early axSpA according to the following inclusion criteria: (1) fulfilment of the ASAS classification criteria for axSpA (4), (2) age over 18 years old, (3) no chronic SIJ lesion, and (4) no contraindication or side effect to NSAIDs. All experiments were conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from each patient. This study was approved by the Institutional Review Board of Armed Forces Medical Command (AFMC-17061-IRB-17-060). This study was registered in www.clinicaltrials.gov under the registration number: NCT03190603.

Biochemical, clinical, and radiologic data were collected at baseline, 6 and 12 weeks after full-dose NSAID treatment (ASAS NSAID index=100) (5). Spondyloarthritis Research Consortium of Canada (SPARCC) inflammation score was measured by two trained rheumatologist (6).

The Friedman test was used to compare continuous values measured at 3 time points, and the Wilcoxon signed rank test was used for post hoc analysis. Spearman's analysis was used to show the correlation between clinical profile and SPARCC score.

Twelve patients (all mem) with axSpA completed the 12-week follow-up. Median age was 21 years old, and median SPARCC inflammation score was 17. The inter-observer correlation coefficients for SPARCC inflammation score at baseline, week 6, and week 12 were 0.986, 0.977, and 0.946, respectively. The total SPARCC inflammation score significantly decreased at 6 and 12 weeks. However, difference between 6 and 12 weeks was not significant. Detailed information of changes in SPARCC score and other clinical/biochemical parameters are shown in Table I. CRP and ESR showed significant correlations with the SPARCC inflammation score (Rho=0.554, p=0.001, Rho = 0.368, p=0.041, respectively).

We demonstrated that an initial 6 weeks of full-dose NSAID therapy could significantly attenuate BMO of the SIJ in early axSpA. Therefore, at least 6 weeks of full-dose NSAID is needed to reverse acute inflammatory lesions, and could provide window period for preventing further structural damage in early axSpA. Additionally, there were significant correlations between SPARCC inflammation score and ESR/CRP. The EULAR recommendation stated that SIJ and spine MRI could provide additional information on axSpA disease activity (7). Kang *et al*. demonstrated correlation between SPARCC inflammation score and ESR/CRP (8), and the present study showed similar results. The aforementioned results could reinforce the recommendation from EULAR, because definite correlations between SPARCC inflammation score and ESR/CRP were proven consistently. Further research with a larger number of patients is needed to clarify the definite beneficial effects of NSAIDs on MRI findings in axSpA.

H.K. MIN[1], *MD*
H. CHO[2], *MD*
S.-H. PARK[1], *MD, PhD*

[1]Division of Rheumatology, Dept. of Internal Medicine, School of Medicine, The Catholic University of Korea, Seoul; [2]Division of Rheumatology, Dept. of Internal Medicine, Armed Forces Capital Hospital, Armed Forces Medical Command, Seongnam, South Korea.

Please address correspondence to:
Dr Sung-Hwan Park,
Division of Rheumatology, Dept. of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Republic of Korea.
E-mail: rapark@catholic.ac.kr

Funding: this work was supported by the Korean Military Medical Research Project funded by the ROK Ministry of National Defense [ROK-MND-2017-KMMRP-012].

Competing interests: none declared.

References

1. VAN DER HEIJDE D, RAMIRO S, LANDEWÉ R *et al*.: 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis* 2017; 76: 978-91.
2. KANG KY, KIM IJ, YOON MA, HONG YS, PARK SH, JU JH: Fat metaplasia on sacroiliac joint magnetic resonance imaging at baseline is associated with spinal radiographic progression in patients with axial spondyloarthritis. *Plos One* 2015; 10: e0135206.
3. PROTOPOPOV M, SIEPER J, HAIBEL H, LISTING J, RUDWALEIT M, PODDUBNYY D: Relevance of structural damage in the sacroiliac joints for the functional status and spinal mobility in patients with axial spondyloarthritis: results from the German Spondyloarthritis Inception Cohort. *Arthritis Res Ther* 2017; 19: 240.
4. SIEPER J, RUDWALEIT M, BARALIAKOS X *et al*.: The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis* 2009; 68 (Suppl. 2): ii1-44.
5. DOUGADOS M, SIMON P, BRAUN J *et al*.: ASAS recommendations for collecting, analysing and reporting NSAID intake in clinical trials/epidemiological studies in axial spondyloarthritis. *Ann Rheum Dis* 2011; 70: 249-51.
6. LANDEWÉ RB, HERMANN KG, VAN DER HEIJDE DM *et al*.: Scoring sacroiliac joints by magnetic resonance imaging. A multiple-reader reliability experiment. *J Rheumatol* 2005; 32: 2050-5.
7. MANDL P, NAVARRO-COMPAN V, TERSLEV L *et al*.: EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. *Ann Rheum Dis* 2015; 74: 1327-39.
8. KANG KY, JUNG JY, HONG YS, JU JH, PARK SH: Positive correlation between inflammation on sacroiliac joint MRI and serum C-terminal telopeptide of type-I collagen in ankylosing spondylitis but not in non-radiographic axial spondyloarthritis. *Clin Exp Rheumatol* 2017; 35: 415-22.

Table I. Comparison of SPARCC inflammation score of SIJ between baseline, 6- and 12-week follow-up.

	Baseline	Follow-up at week 6	Follow-up at week 12	p*	p-value: Baseline to 6 weeks	p-value: Baseline to 12 weeks	p-value: 6 weeks to 12 weeks
SPARCC score of BMO (0-48)	10.2 [9.0; 15.5]	5.0 [3.8; 6.5]	5.5 [1.8; 9.5]	**0.009**	**0.001**	**0.017**	0.833
SPARCC score of intense oedema (0-12)	0.8 [0.0; 2.0]	0.0 [0.0; 0.2]	0.0 [0.0; 0.5]	0.226	0.105	0.144	0.705
SPARCC score of deep oedema (0-12)	3.2 [0.5; 5.8]	0.8 [0.0; 1.2]	0.0 [0.0; 1.5]	**0.049**	**0.008**	0.116	1.000
Total SPARCC inflammation score of SIJ (0-72)	16.8 [11.8; 22.0]	6.0 [3.8; 8.2]	6.5 [1.8; 14.0]	**0.012**	**0.001**	**0.025**	1.000

BMO: bone marrow oedema, MRI: magnetic resonance imaging, SIJ: sacroiliac joint, SPARCC: Spondyloarthritis Research Consortium of Canada. *p-value for Friedman test.