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Original Article

Effect of Disease Duration and Activity and the Treatment Process on Central Sensitization in Patients with Ankylosing Spondylitis

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ABSTRACT

Objective: Ankylosing spondylitis (AS) is a chronic inflammatory disease. Its main symptom is inflammatory low back pain. The presence of central sensitization (CS) in chronic pain conditions has been emphasized in several studies, but there are insufficient studies on AS patients. The aim of this study was to evaluate the relationship between disease activity in AS, the type of pain, and the presence of CS.

Methods: Patients' age, gender, body mass index, disease duration, drugs used in the treatment, pain type and severity, presence of CS disease activity, and quality of life were evaluated.

Results: Evaluation was made on 80 patients, comprising 49 (61.2%) females and 31 (38.8%) males. A statistical significance was found between the presence of CS and high scores of painDETECT, Bath Ankylosing Spondylitis Disease Activity Index, Numerical Rating Scale for pain, Ankylosing Spondylitis Disease Activity Index-sedimentation, Ankylosing Spondylitis Quality of Life Index, low Short-Form-12 (SF-12) physical score ($^{***}p<0.001$), low SF-12 mental score ($^{**}p<0.01$), and increased age ($^{*}p<0.05$).

Conclusion: The results of this study demonstrated that as CS was present in the majority of AS patients, multidirectional evaluation of these patients is required, and in treatment approaches, evaluation is important in respect of treatments for CS in addition to the suppression of inflammation.

INTRODUCTION

Ankylosing spondylitis (AS), which is the most frequently seen type of the spondyloarthropathy disease group, is a chronic inflammatory rheumatological disease characterized by axial and sacroiliac joint involvement. Peripheral joint involvement and extra-articular findings may also be seen. Prevalence has been reported as 0.1%–0.5%, and the female/male ratio as approximately 1:2. In 70%–80% of patients, there is inflammatory low back pain, which is one of the three clinical criteria for AS diagnosis.[1]

The duration of morning stiffness and sensitivity in joint and enthesis regions, in addition to pain, have a significant place in the scales used when making decisions about disease severity and activity and treatment.[2] Many studies have shown that in addition to the nociceptive component of pain, which is inflammatory in nature, there is a neuropathic component. It has been emphasized that pain is

caused directly by the expression of inflammatory mediators by explaining the existing pain in the form of neuroimmune collaboration, and it has been attempted to explain the neuropathic pain component in this way. Wu et al.[3] showed the presence of a neuropathic component in low back pain in AS patients and highlighted the inflammatory–neuropathic pain combination.

In conditions such as AS, when pain has become chronic, sensitization occurs in nociceptors, which play a role in pain signaling. If considered as an adaptation mechanism, pain hypersensitization is characterized by a decrease in the pain threshold and an increase in the amount of response to stimuli above the threshold. If this becomes chronic, it results in nociplastic change, manifesting as a change in the balance between the excitation–inhibition mechanism. As a result of all these changes in the mechanism, the development of central sensitization (CS) in chronic pain conditions can eventually be seen as excitability changes in secondary neurons at the spinal level and in neurons in the supraspinal regions (e.g., thalamus and cortex).[4] Pathan et al.[5] explained the development of CS in spondyloarthropathies with a neuroinflammation mechanism.

The aim of this study was to evaluate disease activity in AS, in which the most important clinical characteristic is pain negatively affecting the daily quality of life of the patient, to determine the type of pain, the frequency of neuropathic pain, the presence of CS, and the relationship between these parameters and CS.

MATERIALS AND METHODS

This cross-sectional, observational pilot study included 80 consecutive AS outpatients. Informed consent was obtained from all the patients. The study inclusion criteria were defined as:

- A diagnosis of AS according to the 2009 ASAS criteria,[6]
- Age in the range of 18–65 years,
- Agreement to participate in the study.

The study exclusion criteria were defined as:

- A diagnosis of another chronic inflammatory or neurological disease which could cause CS,
- Changes in cognitive level or insufficient mental capacity which would prevent responding to the questions asked,
- Age <18 years or >65 years.

A record of age, gender, body mass index (BMI), disease duration, and drugs used during treatment was made for each patient. Evaluation of neuropathic pain was made with the painDETECT test. The presence of CS was evaluated with the CS inventory, and the severity of pain was identified with a Numerical Rating Scale (NRS) for pain. In the evaluation of disease activity, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Ankylosing Spondylitis Disease Activity Index-sedimentation (ASDAS-ESR), and the Ankylosing Spondylitis Quality of Life (ASQoL) Index were used.

Evaluation scales

Numerical Rating Scale (NRS) for Pain

This scale is used in the monitoring of pain and the measurement of pain severity. Patients are asked to mark the severity of pain felt on a 10-cm line marked from 0 to 10, where 0=no pain and 10=the most severe pain.

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

This scale, which is used to evaluate disease activity, is formed of six measurements of fatigue, axial and peripheral joint pain, morning stiffness, and sensitivity. Scoring is made from 0 to 10. A BASDAI score of ≥4 is evaluated as activation.[7] The repeatability and change sensitivity characteristics have been proven with validity and reliability studies of the scale in Turkish.[8]

Ankylosing Spondylitis Disease Activity Index-sedimentation (ASDAS-ESR)

In addition to the spinal and peripheral pain, duration of morning stiffness and global evaluation of 0–10 points used in the BASDAI to evaluate disease activity, evaluation of erythrocyte sedimentation rate as millimeter/hour is added to obtain a score. A score of <1.3 is evaluated as mild disease activity, 1.3–2.1 as moderate disease activity, 2.1–3.5 as high disease activity, and >3.5 as very high disease activity.[9]

Ankylosing Spondylitis Quality of Life (ASQoL) Index

This scale is formed from a total of 18 questions related to the daily life of patients. Each question has a response of yes or no. The number of questions that are given a response of yes is added. A higher number indicates a lower quality of life.[10] Reliability and validity studies of the scale in Turkish were conducted by Duruöz et al.[11]

PainDETECT Questionnaire

This scale is used to evaluate the presence of neuropathic pain in patients.[12] A total questionnaire score of ≤12 is accepted as there being no neuropathic pain component. A total score of 13–18 is accepted as uncertain, but there could be a neuropathic component, and a score of ≥19 is accepted as the presence of a neuropathic pain component. Reliability and validity studies of the scale in Turkish were conducted by Alkan et al.[13]

Short-Form-12 (SF-12) Quality of Life Questionnaire

The SF-12 consists of 12 items in 8 subscales of physical functionality (2 items), physical role (2 items), bodily pain

(1 item), general health (1 item), energy (1 item), social functionality (1 item), emotional role (2 items), and mental health (2 items). The items related to physical and emotional roles are answered with yes or no, and the other items are answered using a Likert-type scale with 3–6 options. The physical component summary-12 (PCS-12) is obtained from the subscales of general health, physical functionality, physical role, and bodily pain, and the mental component summary-12 (MCS-12) is obtained from the subscales of social functionality, emotional role, mental health, and energy. The scores for the PCS-12 and the MCS-12 range from 0 to 100, with higher points indicating better health.[14] Reliability and validity studies of the scale in Turkish were conducted by Soylu and Kütük.[15]

Central Sensitization (CS) inventory

This scale consists of 2 sections: section A evaluating symptoms thought to be related to CS syndromes and section B rapidly questioning whether or not the patient has previously received a specific diagnosis. Section A includes 25 items questioning the frequency of symptoms seen in CS syndromes and is scored from 0 to 100 points. Each symptom is scored according to the frequency experienced as 0: never, 1: rarely, 2: sometimes, 3: often, and 4: always. A higher total score indicates more symptoms related to CS. Section B questions whether or not the patient has been diagnosed with any disease within CS syndromes.[16] This inventory is used for screening and is known to be specific and sensitive for chronic pain patients. Reliability and validity studies of the scale in Turkish were conducted in 2017.[17]

Statistical analysis

The data obtained in the study were analyzed statistically using IBM SPSS v. 22 software. Conformity of the data to normal distribution was assessed with the Kolmogorov–Smirnov and the Shapiro–Wilk tests. Student's t-test was used to compare variables with normal distribution and the Mann–Whitney U test for variables not showing normal distribution. Categorical variables were compared with the Chi-squared test and Monte-Carlo correction. Correlation coefficients were examined to determine relationships between the CS inventory points and other variables. Multiple linear regression analysis was applied with the step-wise regression method to obtain the independent variables most affecting the CS inventory. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The evaluation was made of 80 patients, comprising 49 (61.2%) females and 31 (38.8%) males with a mean age of 44.40±11.34 years, mean BMI of 27.57±5.44, and mean disease duration of 27.97±37.34 months. Of the patients with CS, 39 were females and 12 were males. A statistically significant relationship was determined between age and the presence of CS ($r=0.338$, $p<0.05$). From the blood parameters evaluated, sedimentation was determined as 15.72±11.65 and CRP as 3.42±4.23. In the disease treatment protocol, 14 patients were taking nonsteroidal anti-inflammatory drugs (NSAID), 10 were taking disease-modifying antirheumatic drugs and NSAID, and 56 were taking anti-TNF treatment. No statistically significant relationship was determined between medical treatment and the score of CS ($p>0.05$).

Disease activity and quality of life of the patients were evaluated with BASDAI, ASDAS-ESR, ASQoL, and SF-12 physical and mental scores. When evaluating the ASDAS-ESR, disease activity was classified into four groups. Mild disease was determined in 4 (5%) patients, moderate in 11 (13.8%), high in 36 (45%), and very high in 29 (36.2%). A statistically significant relationship was determined between increased disease activity and diminished quality of life ($r=0.715$, $p<0.05$). A statistically significant relationship was determined between age and ASDAS-ESR ($r=0.248$, $p<0.05$). There was a statistically significant relationship between age and ASQoL ($r=0.364$, $p<0.05$). In

Table 1. Comparison of groups with and without CS

	Patients with CS (n=51)	Patients without CS (n=29)	p[a]
Age	39.34±12.17	47.27±9.85	0.02
BMI	26.06±5.59	28.42±5.21	0.06
Disease duration	7.00 (20.00)	12.00 (44.00)	0.270
NRS	5.00 (3.00)	7.00 (2.00)	<0.001
ASDAS-ESR	2.50 (1.45)	3.50 (0.70)	<0.001
ASQoL	6.00 (5.00)	12.00 (6.00)	<0.001
SF-12 Mental	53.30 (19.73)	41.29 (15.42)	0.009
SF-12 Physical	38.89±9.32	30.12±5.99	<0.001
painDETECT	8.14±5.46	16.71±6.37	<0.001
BASDAI	3.42±1.72	6.08±1.64	<0.001

Data were presented as median (interquartile range) or median±standard deviation. [a]Analyzed by the Mann–Whitney U test or t-test, $p<0.05$.

CS: Central Sensitization; NRS: Numerical Rating Scale; ASDAS-ESR: Ankylosing Spondylitis Disease Activity Index-sedimentation; ASQoL: Ankylosing Spondylitis Quality; BMI: Body mass index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

addition to the NRS for pain evaluation, painDETECT was used to determine the type of pain. Nociceptive pain was determined in 36 (45%) patients, mixed type in 23 (28.7%), and neuropathic pain in 21 (26.3%). In the CS inventory used in the evaluation of pain centralization, a score of >40 showed the presence of CS, which was determined in 51 (63.7%) patients.

In the ASDAS-ESR results as one of the evaluation parameters of disease activity, the presence of CS was not determined in mild disease activity. CS was determined to be present in 3 (5.9%) patients with moderate disease activity, in 23 (45.1%) patients with high disease activity, and in 25 (49.0%) patients with very high disease activity. No statistically significant relationship was determined between disease duration and the score of CS ($p>0.05$). The increase in the NRS and ASQoL values in patients with CS was statistically significant ($p<0.001$). The decrease in the SF-12 mental score values in patients with SS was statistically significant ($p<0.01$). The results are shown in Table 1.

In the painDETECT evaluation of patients with CS present, nociceptive pain was determined in 13 (25.4%), mixed type pain in 19 (37.3%), and neuropathic pain in 19 (37.3%). Mix-type pain and neuropathic pain were statistically significant in the presence of CS ($p<0.05$). The increase in BASDAI scores and the decrease in SF-12 physical scores were statistically significant in patients with CS ($p<0.001$). From the demographic values, statistical significance was found between increased age and the score of CS ($r=0.379$, $p<0.05$), and no significance was seen between CS and BMI ($p>0.05$). No statistically significant relationship was seen between age and neuropathic pain ($p>0.05$). The results are given in Table 1.

The results obtained by applying step-wise regression analysis to variables affecting the CS inventory points are shown in Table 2. According to the results shown in Table 2 there were only three variables that affected the CS inventory score.

In the cutoff points of the CS inventory, the questionnaire variables of age, ASQoL, and painDETECT were significant in the contribution to the model ($p<0.05$). A strongly significant correlation was determined between the variables of age, ASQoL, and painDETECT and the CS inventory points ($r=0.74$), and the three variables explained 56% of the CS inventory points.

Table 2. Results of regression analysis of the CS inventory

Variable	β	S(β)	BETA	VIF	t	p
Fixed	4.055	5.283	–	–	0.768	0.445
Age	0.311	0.118	0.219	1.117	2.646	0.002
ASQoL	1.149	0.361	0.322	1.753	3.181	0.001
painDETECT	0.926	0.208	0.421	1.537	4.443	0.01

ASQoL: Ankylosing Spondylitis Quality of Life; $R=0.746$; $R^2=0.556$; $F(3.76)=31.745$; $p<0.05$; CS inventory=4.055+0.311 age + 1.149 ASQoL + 0.926 painDETECT.

DISCUSSION

CS, which is referred to in the literature with different names such as central pain syndrome, central pain, and diffuse pain, forms with the interaction of spinal and supraspinal pain signaling in chronic pain pathologies. When the current clinical status is considered in AS patients, as pain plays an important role even when evaluating inflammation and disease activity, the importance of CS evaluation in these patients becomes more predominant.

Epidemiological studies have reported the frequency of CS present in the general population to be 5%–15% (the majority consisting of fibromyalgia syndrome) and 10%–30% in spondyloarthropathies. In AS patients meeting fibromyalgia diagnostic criteria, the frequency has been reported to be 13%–20%.[18] There are several clinical studies in the literature showing the presence of CS in chronic pain conditions. In a review that evaluated the relationship with chronic low back pain, there were physiological changes at the supraspinal level, an increase in cortical activity, and neuroplastic changes in the brain when CS was seen to be present in imaging studies. This was explained as the emergence of clinical findings such as allodynia, hyperalgesia, and disinhibition of the inhibitor mechanism, and lack of a sufficient increase in blood flow in the periaqueductal gray matter as a response given to painful stimuli.[19] In the current study, the presence of CS determined in 63.7% of the patients was found to be statistically significantly high. A statistically significant relationship was determined between the elevated CS scores and an increase in disease activity, a decrease in mental and physical health affecting quality of life, and the presence of mix-type pain and neuropathic pain.

In chronic pain conditions such as, modulation occurs through the role taken by inflammatory mediators in both the peripheral and central nervous systems.[4] At the same time, there has been a neuropathic pain component in addition to the inflammatory component in AS. Epidemiological studies have reported the frequency of neuropathic pain in the general population to be 7%–8% and 20%–25% in individuals with chronic pain.[20] If accompanying chronic low back pain is considered, previous studies have shown a wide range of 16%–54% of the frequency of neuropathic pain seen in AS patients.[21]

In a study of 105 AS patients by Choi et al.,[22] a significant relationship was found between neuropathic pain and an increase in age and disease duration. Kim et al.[21] evaluated AS studies, which used painDETECT as the evaluation scale of neuropathic pain, and obtained the data of four studies in which it was seen that in AS patients with neuropathic pain, there was high pain severity, high disease activity, and diminished quality of life. However, no consensus was reached on the relationship between neuropathic pain and age and disease severity in AS patients. In the current study, neuropathic pain was present in 26.3% of the patients. There was a significant relationship between disease duration and neuropathic pain, but no significance

was determined with age. A statistically significant relationship was determined between pain severity, increased disease activity, decreased mental and physical scores of quality of life, and the presence of CS and neuropathic pain.

Abnormal ectopic activity in nociceptive nerves, peripheral and central sensitization, impaired inhibitor modulation, and pathological activation of microglia can be included among the mechanisms forming neuropathic pain.[23] In a study of 105 AS patients, Tuba et al.[24] examined the presence of CS and found statistically significantly high scores in the questionnaire that evaluated neuropathic pain in patients with CS, which supported the results of the current study. In the same study, the combination of increased age, disease duration, disease activity, female gender, and high BMI with CS was emphasized. In the current study, increased age, female gender, and high disease activity were statistically significantly correlated with CS. Therefore, the combination with neuropathic pain during the evaluation of CS must not be forgotten, and the fact that the presence of CS was found to be statistically significantly high in the current study patients supports these data. In the regression analysis, the data obtained from increased neuropathic pain scale values in AS patients with neuropathic pain could be a finding for the presence of CS. Similarly, the high age and ASQoL results used in the evaluation of the quality of life are important as a clue to the development of CS.

The main aim of pain treatment in AS is to suppress inflammation, but despite the treatments given, there are many patients for whom inflammation is suppressed but who continue to have complaints of persistent pain and do not experience relief. Clinical studies of AS patients have shown that pain and inflammation are not always correlated with data obtained from blood parameters and radiological imaging methods.

In the evaluation of pain in AS, the neuropathic component must not be forgotten, and the definition of neuroinflammation must be kept in mind.[25] A case was reported of a 72-year old diagnosed with AS, whose treatment for opioid-resistant pain started with pregabalin and the management of pain and comorbid psychiatric symptoms, which was seen to be potentially useful in the treatment of withdrawal symptoms after terminating opioids.[26] In another study of 88 AS patients, 44 patients started treatment with amitriptyline and 44 started placebo treatment. Then, the evaluation was made of pain, functional capacity, sleep, and fatigue, and a decrease in BASDAI score, decreased pain, and improved sleep quality in the patients using amitriptyline were observed.[27]

When the medical agents used in treatment (e.g., selective serotonin reuptake inhibitors, tricyclic antidepressants, or gabapentinoids) were evaluated in the presence of CS, the approach was seen to be completely different from the inflammation inhibition-focused treatment method in AS treatment, and the high rate of CS positivity determined in the current study explained as a change in pain perception, demonstrating the importance of a multidirectional approach in patient evaluation.[28] There are also studies in the literature showing that in addition to medical treatment for chronic pain and CS, a regular lifestyle, healthy eating, and eliminating stress have positive effects by forming a negative effect on neuroinflammation.[29,30]

There remains the question of why CS is seen in some AS patients, where the pain is predominant, and not in other AS patients with the same demographic and clinical characteristics. When evaluating patients, it must not be forgotten that they are bio-psychosocial beings. In addition to the pathology, not only laboratory parameters but also social surroundings and psychological factors can create differences in an individual's perception of pain. When the questions in the CS inventory are taken into consideration, the importance of making treatment decisions by multidirectional evaluations becomes more evident. This has been emphasized in this study by the high rate of CS presence. Limitations of this study could be said to be the relatively low number of patients and that no psychological assessment of the patients was made during the CS evaluation.

Ethics Committee Approval

This study approved by the Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee (Date: 23.06.2021, Decision No: 2021–06/19).

Informed Consent

Prospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: E.G., A.D., E.G., H.A.U., S.H.; Design: E.G., A.D., E.G., H.A.U., S.H.; Supervision: E.G.; Fundings: E.G., A.D., E.G., H.A.U., S.H.; Data: E.G., A.D.; Analysis: E.G., E.G.; Literature search: E.G.; Writing: E.G.; Critical revision: E.G., S.H.

Conflict of Interest

None declared.

REFERENCES

1. Wang R, Ward MM. Epidemiology of axial spondyloarthritis: an update. Curr Opin Rheumatol 2018;30:137–43. [CrossRef]
2. Zochling J. Measures of symptoms and disease status in ankylosing spondylitis: Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), and Health Assessment Questionnaire for the Spondylarthropathies (HAQ-S). Arthritis Care Res (Hoboken) 2011;63:S47–58.
3. Wu Q, Inman RD, Davis KD. Neuropathic pain in ankylosing spondylitis: a psychophysics and brain imaging study. Arthritis Rheum 2013;65:1494–503. [CrossRef]
4. Bidad K, Gracey E, Hemington KS, Mapplebeck JCS, Davis KD,

Inman RD. Pain in ankylosing spondylitis: a neuro-immune collaboration. Nat Rev Rheumatol 2017;13:410–20. [CrossRef]
5. Pathan EMI, Inman RD. Pain in spondyloarthritis: A neuro-immune interaction. Best Pract Res Clin Rheumatol 2017;31:830–45.
6. Sieper J, van der Heijde D, Landewe R, Brandt J, Burgos-Vagas R, Collantes-Estevez E, et al. New criteria for inflammatory back pain in patients with chronic back pain: a real patient exercise by experts from the Assessment of SpondyloArthritis international Society (ASAS). Ann Rheum Dis 2009;68:784–8. [CrossRef]
7. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21:2286–91.
8. Akkoc Y, Karatepe AG, Akar S, Kirazli Y, Akkoc N. A Turkish version of the bath ankylosing spondylitis disease activity index: reliability and validity. Rheumatol Int 2005;25:280–4. [CrossRef]
9. Lukas C, Landewe R, Sieper J, Dougados M, Davis J, Braun J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:18–24.
10. Doward LC, Spoorenberg A, Cook SA, Whalley D, Helliwell PS, Kay LJ, et al. Development of the ASQoL: A quality of life instrument specific to ankylosing spondylitis. Ann Rheum Dis 2003;62:20–6.
11. Duruöz M, Doward L, Turan Y, Cerrahoglu L, Yurtkuran M, Calis M, et al. Translation and validation of the Turkish version of the Ankylosing Spondylitis Quality of Life (ASQOL) questionnaire. Rheumatol Int 2013;33:2717–22. [CrossRef]
12. Freynhagen R, Baron R, Gockel U, Tolle TR. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin 2006;22:1911–20.
13. Alkan H, Ardic F, Erdogan C, Sahin F, Sarsan A, Findikoglu G. Turkish version of the painDETECT questionnaire in the assessment of neuropathic pain: a validity and reliability study. Pain Medicine 2013;14:1933–43. [CrossRef]
14. Ware Jr J, Kosinski M, Keller S. SF-12: how to score the SF-12 physical and mental health summary scales. Boston: QualityMetric Inc. Health Assessment Lab; 2002.
15. Soylu C, Kütük B. SF-12 Yaşam Kalitesi Ölçeği'nin Türkçe formunun güvenirlik ve geçerlik çalışması. Türk Psikiyatri Dergisi. 2021 Jan 31. Doi: 10.5080/u25700. [Epub ahead of print]. [CrossRef]
16. Mayer TG, Neblett R, Cohen H, Howard KJ, Choi YH, Williams MJ, et al. The development and psychometric validation of the central sensitization inventory. Pain Pract 2012;12:276–85.
17. Keleş ED, Birtane M, Ekuklu G, Kılınçer C, Çalıyurt O, Taştekin N, et al. Validity and reliability of the Turkish version of the central sensitization inventory. Arch Rheumatol 2021;36:518–26.
18. Dydyk AM, Givler A. Central pain syndrome. StatPearls. Treasure Island (FL)2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK553027/. Accessed Aug 19, 2022.
19. Sanzarello I, Merlini L, Rosa MA, Perrone M, Frugiuele J, Borghi R, et al. Central sensitization in chronic low back pain: A narrative review. J Back Musculoskelet Rehabil 2016;29:625–33. [CrossRef]
20. Bouhassira D, Lanteri-Minet M, Attal N, Laurent B, Touboul C. Prevalence of chronic pain with neuropathic characteristics in the general population. Pain 2008;136:380–7.
21. Kim TW, Son SM, Lee JS. Neuropathic pain in ankylosing spondylitis: a meta-analysis. Z Rheumatol 2020;79:95–102. [CrossRef]
22. Choi JH, Lee SH, Kim HR, Lee KA. Association of neuropathic-like pain characteristics with clinical and radiographic features in patients with ankylosing spondylitis. Clin Rheumatol 2018;37:3077–86.
23. Xu L, Zhang Y, Huang Y. Advances in the treatment of neuropathic pain. Adv Exp Med Biol 2016;904:117–29. [CrossRef]
24. Tuba K, Göğebakan H, Çetin G. Should central sensitization and neuropathic pain be considered in disease activity and treatment decision in axial ankylosing spondilitis? Cukurova Med J 2019;44:1–10.
25. Borman P, Kaygisiz F, Yaman A. Neuropathic component of low back pain in patients with ankylosing spondylitis. Mod Rheumatol 2021;31:462–7. [CrossRef]
26. Kontoangelos KA, Kouzoupis AV, Ferentinos PP, Xynos ID, Sipsas NV, Papadimitriou GN. Pregabalin for opioid-refractory pain in a patient with ankylosing spondylitis. Case Rep Psychiatry 2013;2013:912409. [CrossRef]
27. Koh WH, Pande I, Samuels A, Jones SD, Calin A. Low dose amitriptyline in ankylosing spondylitis: a short term, double blind, placebo controlled study. J Rheumatol 1997;24:2158–61.
28. Nijs J, Leysen L, Vanlauwe J, Logghe T, Ickmans K, Polli A, et al. Treatment of central sensitization in patients with chronic pain: time for change? Expert Opin Pharmacother 2019;20:1961–70. [CrossRef]
29. Allison DJ, Thomas A, Beaudry K, Ditor DS. Targeting inflammation as a treatment modality for neuropathic pain in spinal cord injury: a randomized clinical trial. J Neuroinflammation 2016;13:152.
30. Schuh-Hofer S, Wodarski R, Pfau DB, Caspani O, Magerl W, Kennedy JD, et al. One night of total sleep deprivation promotes a state of generalized hyperalgesia: a surrogate pain model to study the relationship of insomnia and pain. Pain 2013;154:1613–21.

Ankilozan Spondilit Hastalarında Hastalık Süresi, Aktivitesi Ve Tedavi Sürecinin Santral Sensitizasyon Üzerine Etkisi

Amaç: Ankilozan spondilit (AS), kronik inflamatuvar bir hastalıktır ve inflamatuvar bel ağrısı ana semptomdur. Mevcut ağrının nosiseptif yanında nöropatik komponenti ile ilgili çalışmalar mevcuttur. Kronik ağrılı durumlarda santraL sensitizasyon (SS) varlığı çeşitli hastalıklarda vurgulanmaktadır ancak AS'li hastalarda yeterli çalışma bulunmamaktadır. Bizim amacımız AS'de hastalık aktivitesi,ağrı tipi, SS varlığını ve ilişkilerini değerlendirmektir.

Gereç ve Yöntem: Hastalar yaş, cinsiyet, vücut kitle indeksi, hastalık süresi, tedavide kullanılan ilaçlar, ağrı tipi ve şiddeti, SS varlığı, hastalık aktivitesi ve yaşam kalitesi açısından değerlendirildi.

Bulgular: Çalışmaya 49 (%61.3) kadın, 31 (%38.8) erkek toplam 80 hasta AS hastası dahil edildi. PainDETECT, BASDAI, NRS, ASDAS-ESH, ASQoL skorlarında yükseklik, ve SF-12 fiziksel skorunda düşme($p<0.001^{***}$), SF-12 mental skorunda düşme ($p<0.01^{**}$) ve yaş artışı ($p<0.05^{*}$) ile SS varlığı arasında istatistiki olarak anlamlılık tespit edildi.

Sonuç: Bizim çalışmamız, AS tanılı hastalarda SS varlığının çokluğunun, hastaların hem çok yönlü değerlendirilmesi gerektiği, hem de tedavi yaklaşımında sadece inflamasyonun baskılanması yanında SS'e yönelik tedavilerin eklenmesi yönünde değerlendirilmesinin önemini vurgulamaktadır.

Anahtar Sözcükler: Ankilozan spondilit; hastalık aktivitesi; hastalık süresi; santral sensitizasyon.