Observational Study

# The Effect of Central Sensitization on Interlaminar Epidural Steroid Injection Treatment Outcomes in Patients with Cervical Disc Herniation: An Observational Study

Rekib Sacaklidir, MD[1], Canan Sanal-Toprak, MD[2], Feyza Nur Yucel, MD[3], Osman Hakan Gunduz, MD[1], and Savas Sencan, MD[1]

From: [1]Division of Pain Medicine, Department of Physical Medicine and Rehabilitation, Marmara University School of Medicine, Istanbul, Turkey; [2]Department of Physical Medicine and Rehabilitation, Marmara University School of Medicine, Istanbul, Turkey; [3]Department of Physical Medicine and Rehabilitation, Boyabat 75th Year State Hospital, Sinop, Turkey

Address Correspondence:
Rekib Sacaklidir, MD
Division of Pain Medicine, Department of Physical Medicine and Rehabilitation, Marmara University School of Medicine
Muhsin Yazıcıoğlu Cd No:10
34899 Pendik/İstanbul,Turkey
E-mail:
rakipsacakli@hotmail.com

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 01-27-2022
Revised manuscript received: 03-27-2022
Accepted for publication: 04-13-2022

Free full manuscript:
www.painphysicianjournal.com

**Background:** Central sensitization (CS) is a hyperexcitability that is manifested by the increased response of the central nervous system to sensory stimuli. It has been shown that the presence of CS may have a negative effect on the clinical picture in some musculoskeletal diseases and also have a negative effect on spinal procedures.

**Objectives:** To investigate the effect of CS on interlaminar epidural steroid injection (ILESI) treatment outcomes in patients with cervical disc herniation (CDH).

**Study Design:** An observational study.

**Setting:** A university hospital pain management center.

**Methods:** Patients, who underwent ILESI between 2020-2021 due to CDH, were included in the study. The Numeric Rating Scale (NRS-11), Neck Pain and Disability Scale (NPDS), Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS), and Short Form-12 (SF-12) were used for evaluation of patients. Patients were assessed before the procedure, at the first hour, and 3 months after the procedure. The presence of CS was investigated by the Central Sensitization Inventory (CSI).

**Results:** A total of 51 patients were included in the study. Twenty-three of the patients had CS, as assessed by the CSI. Although, patients who underwent ESI, had significantly lower NRS-11, S-LANSS, and NPDS scores, and higher SF-12 scores at all follow-up points. The first and third months, NRS-11, S-LANSS, and NPDS were significantly higher, and SF-12 scores were lower in the CS group compared to patients without CS.

**Limitations:** The short follow-up period and relatively low number of patients can be considered as a limitation. The fact that CS is not evaluated with a more objective method, such as Quantitative Sensory Testing (QST), can be considered as another limitation. Since most clinicians use CSI, so from a "real world" perspective the lack of QST may be observed as a strength of the study. The third limitation is that we did not evaluate the patients' pre- and posttreatment analgesic consumption. Finally, we did not include patients with a history of psychiatric illness, but not evaluating the current psychiatric conditions of the patients could be considered a limitation. Nevertheless, the main strengths of this study are its prospective design and, to our knowledge, it is the first study to explore the effects of CS on cervical ESI treatment.

**Conclusions:** The presence of CS has a negative effect on pain scores, disability, and quality of life in patients undergoing cervical ESI due to CDH.

**Key words:** Cervical disc herniation, epidural injections, central sensitization, central sensitization inventory, neck pain, treatment success, interlaminar, steroids

**Pain Physician 2022: 25:E823-E829**

Cervical disc herniation (CDH) is one of the leading causes of neck pain, and radicular symptoms accompany axial pain in about half of patients (1). The pathophysiology of pain associated with herniation is thought to occur due to increased inflammation due to mechanical compression of the nerve root (2). Treatment options for CDH include conservative treatment, interventional pain procedures, and surgical treatment. Interventional procedures are often the preferred treatment method for people who do not respond to conservative treatments (3). Epidural steroid injection (ESI) is the preferred interventional procedures and has been reported to provide analgesia by reducing epidural and perineural inflammation (4).

Central sensitization (CS) is hyperexcitability that is manifested by the increased response of the central nervous system to sensory stimuli (5). It has been shown that the presence of CS may have a negative effect on the clinical picture in some musculoskeletal diseases and may also have a negative effect on spinal procedures (6-8). Quantitative Sensory Testing (QST) is one of the frequently preferred methods for diagnosing CS and usually includes mechanical, thermal, or pressure pain threshold and temporal summation measurement. Although the QST is valuable in CS research, the Central Sensitization Inventory (CSI) has increasingly been preferred for this purpose due to its easier applicability and low cost in recent years (9). There are few studies on CS and treatment success in interventional pain procedures, and it has been reported that preprocedural QST can be a guide in predicting lumbar ESI treatment response (10). Similarly, a high preoperative CSI score was associated with poor postoperative quality of life, disability, and increased length of hospital stay in patients undergoing spinal fusion (8). It is known that CS is associated with poor recovery of pain, and it seems possible to predict treatment response with CSI (11). Studies (10,12) regarding the effect of CS on ESI outcomes are limited to lumbar radiculopathy, and as we know similar relationship has not yet been demonstrated in patients with CDH. This study aimed to investigate the effect of preprocedural CSI scores on treatment response in patients with CDH who underwent cervical interlaminar ESI (ILESI). We hypothesized that increased pre-procedural CSI scores are associated with poor treatment response in these patients.

## Methods

### Design and Study Population

The study was granted approval from the ethics committee (approval number: 09.2019.1055) and was conducted according to the Declaration of Helsinki principles. It was conducted prospectively with 51 CDH patients who underwent ILESI between 2020 and 2021. Patients, aged 18-75 years, who applied to the pain medicine outpatient clinic, had axial neck and unilateral radicular extremity pain for at least 3 months, and were diagnosed with protruded disc herniation by magnetic resonance imaging were included in the study. Patients with systemic inflammatory disease, bleeding diathesis, history of psychiatric illness, malignancy, contrast material or local anesthetic agent allergy, cervical spinal stenosis, history of cervical ESI, or neck surgery in the last 3 months were excluded from the study. ESI was performed in patients who could not provide adequate analgesia despite conservative treatment (posttreatment Numeric Rating Scale [NRS-11] > 4). Verbal and written consent were obtained from all patients.

### Measures

The NRS-11, Neck Pain and Disability Scale (NPDS), Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS), and Short Form-12 (SF-12) were used for evaluation of patients. The patients were assessed 3 times in total: before the procedure, and at the first and third months after the procedure. The presence of CS was investigated by CSI.

The NRS-11 is where pain is expressed between 0 and 10. Zero means no pain, and 10 means the worst pain.

The NPDS is a 20-item scale developed for patients with neck pain. This scale measures the severity of neck pain, neck movement limitation, its effect on mood and cognition, and the degree of difficulty in activities of daily living. It has been reported to have a high level of reliability and construct validity, as well as being understandable and easily applicable (13). Each item is scored between 0-5, and the total score ranges from 0-100, with higher scores being associated with increased disability. The validity and reliability of the scale in the Turkish population was demonstrated by Biçer et al (14).

S-LANSS is a 7-item scale developed by Bennett et al (15), in 2001, to detect the neuropathic component of pain. The scale consists of 2 parts: the first includes the questioning of sensory complaints, and the second part includes a brief sensory assessment. The total scores range from 0-24, and patients with a score of 12 and above are considered to have neuropathic pain. It has been reported that the Turkish version of the questionnaire has a high level of validity (15).

The SF-12 questionnaire is an abbreviated version of the self-reported 36-Item Short Form Health Survey that is used to assess quality of life. There are 2 scoring systems, mental component score (MCS-12) and physical component score (PCS-12), that have sufficient validity and reliability in evaluating mental and physical well-being. Test scores range from 0-100, with higher scores indicating better quality of life (16).

In 2011, the CSI was developed by Mayer et al (17) to detect CS in patients with chronic pain. The scale consists of 25 somatic and psychosocial symptoms, and the total score varies between 0-100. Patients with 40 points or more are considered CS. The Turkish version of the CSI has been reported to have high sensitivity and specificity, as well as high internal consistency and test-retest reliability (18).

### Injection Technique

The patient was placed in the prone position and cutaneous anesthesia was performed with 3 mL of 2% prilocaine using the sterile technique. After imaging the C7-T1 space with fluoroscopy, it was entered from the right/left paramedian part of the C7-T1 space with an 18G Touhy needle, and the C-arm was set in the contralateral oblique position for depth determination. Under intermittent fluoroscopic imaging, the needle was advanced, and access to the epidural space was confirmed by the loss of resistance technique. Afterwards, the epidural spread was controlled with a contrast agent, and a mixture of 10 mg dexamethasone, 1 mL 2% lidocaine hydrochloride, and 1 mL 0.9% saline was applied to the epidural space. The patient was discharged with recommendations after being kept under observation for 2 hours post-procedure. All injections were performed by the same pain medicine specialist who had at least 5 years of experience.

### Statistical Analyses

Statistical analyses were performed using SPSS version 20.0 software (IBM Corporation, Armonk, NY). Categorical variables were expressed as number and frequency, while mean (standard deviation) and median (interquartile range) were used to define the continuous variables. A chi-square test was used for comparison of categorical variables. The Shapiro-Wilk test was used for the conformity of quantitative data to normal distribution. The Mann-Whitney U and independent t tests were used in the analysis of nonnormally distributed data and in the comparison of normally distributed data, respectively. The changes over time with treatment for nonnormally distributed data were determined by the Friedman test, and repeated measures analysis of variance was used for normally distributed data. Paired sample t test and Wilcoxon signed tests were performed for pairwise comparisons with a Bonferroni correction for multiple comparisons. Statistical significance was accepted at the a $P$ value < 0.017 for Bonferroni correction; otherwise, the $P$ value < 0.05 was considered statistically significant with a 95% confidence interval.

## Results

A total of 51 patients were included in the study. Twenty-three of the patients had CS, as assessed by CSI. The ESI procedure was applied to all patients at C7-T1 level and no major complications were observed. There was no significant difference between the 2 groups in terms of sociodemographic and clinical characteristics, such as age, gender, body mass index, and symptom duration (Table 1). All patients had significantly lower NRS-11, S-LANSS pain scale, and NPDS scores at all follow-up points, and PCS-12 scores were higher than baseline (Figs. 1 and 2).

The initial neck NRS-11 score was found to be significantly higher in patients with CS compared to patients without CS, while the NRS-11 score for arm pain was similar between groups. Post-intervention NRS-11 scores for neck and arm pain at first and third months were significantly higher in patients with CS. NRS-11 scores were significantly improved at all follow-up points when compared to the baseline in both groups (Table 2). Although

Table 1. *CS according to sociodemograpic and clinical characteristics of patients.*

| | Total Cohort | CS | | *P* value |
|---|---|---|---|---|
| | | No | Yes | |
| Age (y) | 47.53 (10.92) | 47.38 (10.67) | 47.64 (10.54) | 0.935* |
| BMI (kg/m$^2$) | 27 (4.46) | 26.21 (3.39) | 27.64 (5.14) | 0.257* |
| Symptom duration (mo) | 12 (6-24) | 12 (3-48) | 12 (3-48) | 0.471† |
| Gender (%) | | | | 0.09‡ |
| Women | 32 (62.8) | 15 (53.5) | 17 (74) | |
| Men | 19 (37.2) | 13 (46.5) | 6 (26) | |

Data presented as mean SD, median IQR, or n (%).
Abbreviations: CS, central sensitization; BMI, body mass index; SD, standard deviation; IQR, interquartile range.
* Independent-Samples t test.
† Mann-Whitney U test.
‡ Pearson chi-square test.

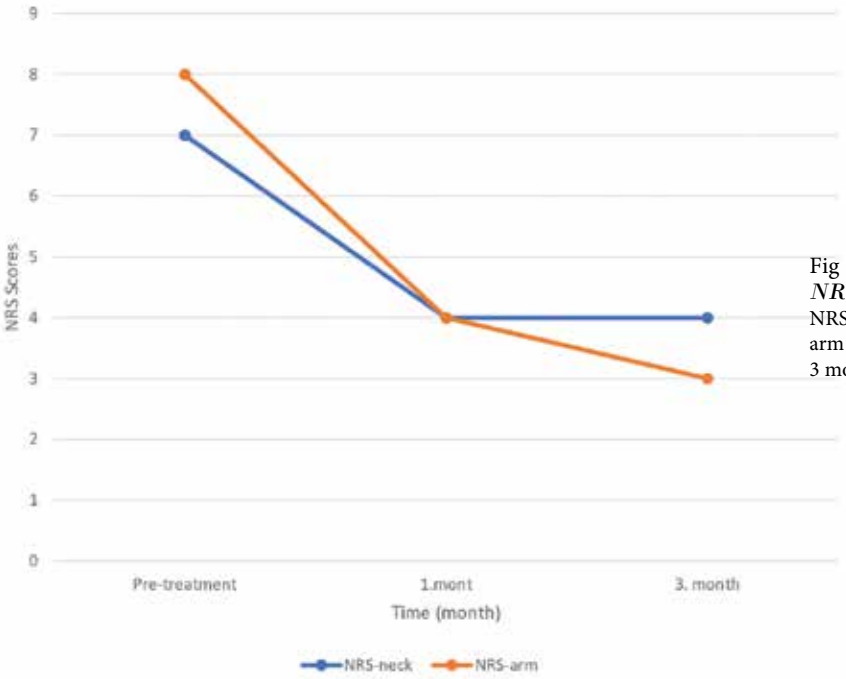


Fig 1. ***Pre- and post-procedural NRS-11 scores.***
NRS-11, numeric rating scale; Neck and arm NRS-11, Pre vs 1 month and Pre vs 3 month are significant ($P < 0.001$).

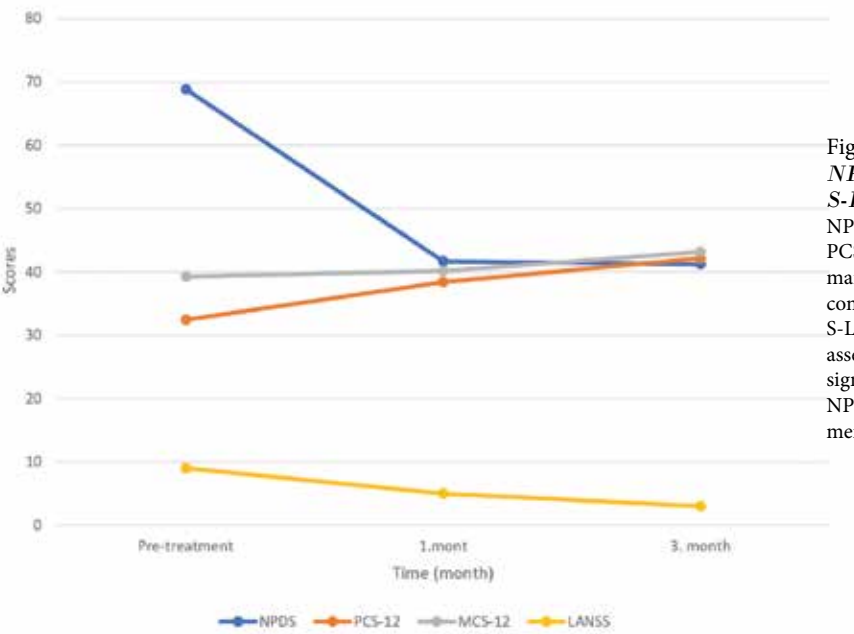


Fig 2. ***Pre- and post-procedural NPDS, PCS-12, MCS-12, and S-LANSS scores.***
NPDS, neck pain and disability scale; PCS-12, physical component summary of short form-12; MCS-12, mental component summary of short form-12; S-LANSS, the self-administered Leeds assessment of neuropathic symptoms and signs significant difference was detected in NPDS, PCS-12, and S-LANSS after treatment ($P < 0.05$).

the initial and post-intervention NPDS scores were significantly higher in the patients with CS compared to patients without CS, NPDS scores were significantly reduced at all follow-up points in both groups (Table 3). All of the MCS-12 scores and post-intervention PCS-12 scores were significantly higher in patients without CS. The PCS-12 score was significantly increased at third month when compared to baseline in patients without CS. There were no improvements in PCS-12 and MCS-12 scores in patients with CS and MCS-12 scores in patients

Table 2. *NRS-11 scores for neck and arm pain according to CS.*

| | CS | | *P* value |
|---|---|---|---|
| | Yes | No | |
| NRS-11-neck | Median (IQR) | Median (IQR) | |
| Pre | 8 (7-8) | 6 (5-8) | 0.016* |
| 1 month | 4 (3-6) | 1 (1-4) | < 0.001* |
| 3 months | 4 (3-6) | 2 (1-4) | < 0.001* |
| *P* value | < 0.001‡ | < 0.001‡ | |
| Pre vs 1 month | < 0.001† | < 0.001† | |
| Pre vs 3 months | < 0.001† | < 0.001† | |
| NRS-11-arm | | | |
| Pre | 8 (7-8) | 8 (6-9) | 0.684* |
| 1 month | 4.5 (3.25-3.26) | 1 (1-4) | 0.001* |
| 3 months | 4.5 (3-7) | 2 (1-4) | 0.001* |
| *P* value | < 0.001‡ | < 0.001‡ | |
| Pre vs 1 month | < 0.001† | < 0.001† | |
| Pre vs 3 months | < 0.001† | < 0.001† | |

Abbreviations: NRS-11, numeric rating scale; CS, central sensitization; IQR, interquartile range.
* Mann-Whitney U test.
‡ Friedman test.
† Wilcoxon sign test.

Table 3. *NPDS scores according to CS.*

| NPDS | CS | | *P* value |
|---|---|---|---|
| | Yes | No | |
| | Mean (SD) | Mean (SD) | |
| Pre | 73.46 (13.64) | 63.26 (14.20) | 0.012* |
| 1 month | 56.80 (18.54) | 25.26 (17.85) | < 0.001* |
| 3 months | 61.08 (17.57) | 20.47 (13.54) | < 0.001* |
| *P* value | 0.002‡ | < 0.001‡ | |
| Pre vs 1 month | < 0.001† | < 0.001† | |
| Pre vs 3 months | 0.010† | < 0.001† | |

Abbreviations: NPDS, neck pain and disability scale; CS, central sensitization; SD, standard deviation; ANOVA, analysis of variance.
* Independent-Samples t test.
‡ Repeated Measure ANOVA.
† Paired-Samples t test.

Table 4. *MCS-12, PCS-12, and S-LANSS scores according to CS.*

| | CS | | *P* value |
|---|---|---|---|
| | Yes | No | |
| MCS-12 | Median (IQR) | Median (IQR) | |
| Pre | 36.90 (30.28-42.74) | 41.28 (36.34-48.98) | 0.036* |
| 1 month | 38.85 (34.89-44.74) | 42.29 (38.07-56.42) | 0.027* |
| 3 months | 37.91 (29.32-43.12) | 46.83 (42.98-56.49) | 0.001* |
| *P* value | 0.290‡ | 0.245‡ | |
| PCS-12 | | | |
| Pre | 30.33 (27.06-37.28) | 33.52 (29.37-43.17) | 0.094* |
| 1 month | 33.27 (30.20-38.40) | 42.56 (37.71-56.58) | < 0.001* |
| 3 months | 32.02 (28.20-43.40) | 49.94 (41.56-50.90) | 0.004* |
| *P* value | 0.701‡ | 0.010‡ | |
| Pre vs 1 month | - | 0.019† | |
| Pre vs 3 months | - | 0.014† | |
| S-LANSS | | | |
| Pre | 11 (6-14) | 8(5-11) | 0.037* |
| 1 month | 8 (3-13) | 1 (0-8) | 0.007* |
| 3 months | 8 (7-8) | 0.5 (0-6.5) | 0.037* |
| *P* value | 0.005 | < 0.001 | |
| Pre vs 1 month | 0.020 | 0.001† | |
| Pre vs 3 months | 0.005 | 0.001† | |

Abbreviations: MCS-12, mental component summary of short form-12; PCS-12, physical component summary of short form-12; S-LANSS, the self-administered Leeds assessment of neuropathic symptoms and signs; CS, central sensitization; IQR, interquartile range.
* Mann-Whitney U test.
‡ Friedman test.
† Wilcoxon sign test.

without CS at any time points. The S-LANSS scores were significantly higher in patients with CS than in patients without CS at any time point, and scores were significantly reduced at 3 months in patients with CS and at 1 and 3 months in patients without CS (Table 4).

## Discussion

CS has been hypothesized to be secondary to dysregulation in the central nervous system, leading to neuronal hyperexcitability and pain (19). Various studies (8,20) have shown that CS has a negative effect on treatment success. It was aimed to show that increased CSI scores are associated with poor treatment response in cervical ESI. In the present study, patients who underwent ESI had significantly lower NRS-11, S-LANSS, and NPDS scores, and higher PCS-12 scores at all follow-up points. The initial NRS-11, S-LANSS, and NPDS scores for neck and arm pain were found to be significantly higher in patients with CS and, after treatment, these scores were found to be significantly higher in patients with CS.

Transforaminal and interlaminar methods are used to reach the epidural space for neck/arm pain due to CDH. ILESI is safer as the arterial structure is less damaged during the procedure, and it is easy to reach the epidural space (21). For this reason, first ILESI was planned for our patients. In the literature, cervical ILESI have been shown to be effective in patients with CDH (22,23). ESI exerts anti-inflammatory effects by reducing cytokines and chemokines, reducing or inhibiting neuroglial activation, inhibiting nociceptive C-fiber conduction, and ectopic neuronal discharge (24). In the present study, it was found that pain, disability, and quality of life scores improved significantly at the first month and third month after ESI compared to pretreatment. This result has shown that ESI is a short-to-moderate effective in CDH-induced neck/arm pain.

Previous studies (8,20,25,26) have shown that patients with CS have higher pain scores and adversely affect posttreatment pain scores. According to Ohashi et al (27), CSI scores were significantly correlated with pain in hip osteoarthritis patients at rest, and they also increased the persistence of postoperative pain in these patients. In patients who underwent total knee arthroplasty, pain scores were found to be significantly higher in the group with CS before treatment, and pain scores were found to be higher in the CS group at the 3-month follow-up after arthroplasty (26). According to Neblett et al (25), CSI was a treatment outcome measure of pain intensity and pain-related anxiety for patients with chronic spinal disorder in a functional restoration program. In the present study, we found that the NRS-11 and S-LANSS scores were significantly higher in the CS group before ESI, and these scores were significantly higher in the CS group at the post-treatment follow-up. Although the effect on pain is complex, we believe that some mechanisms may explain this effect. Some of these mechanisms are a constantly changing mosaic of alterations in membrane excitability, reducing inhibitory transmission, and increasing synaptic efficacy, mediated by many molecular players on a background of phenotypic switches and structural alterations (19).

CS has also been shown to have a negative effect on disability (20,28). According to Kondo et al (20), CSI had a significant effect on the Neck Disability Index in patients with cervical degeneration. In another study, the CSI score demonstrated a moderate correlation with disability in patients with elective spine surgery (28). In the present study, although NPDS scores were significantly reduced at all follow-up points in both groups, the initial and post-intervention NPDS scores was were significantly higher in the patients with CS. Since pre- and posttreatment pain scores were higher in the CS group, disability was expected to be higher in this group. This effect can be explained by a relationship between the severity of pain and dysfunction; therefore, people try to reduce severe pain with functional limitations or become unable to function due to pain (29).

In the present study, there was no change in the mental and physical components of SF-12 after treatment in the CS group; in the non-CS group, there was a significant improvement in the physical scores of SF-12 in the follow-ups. The reason there was no statistical difference in mental functions in the non-CS group may be due to the short follow-up period. However, a significant difference was found in SF-12 values between the CS and non-CS groups before and after treatment. Preoperative CS was found to be associated with worse quality-of-life outcomes following spinal fusions (8). In another study (30), it was stated that the presence of CS in patients who underwent total knee arthroplasty adversely affected the quality of life. These results suggest that the quality of life of patients with CS is impaired, and it is thought that this impairment may be related to disability and pain.

The short follow-up period and relatively low number of patients can be considered a limitation. The fact that CS is not evaluated with a more objective method, such as QST, can be considered another limitation. Since most clinicians use CSI, so from a "real world" perspective the lack of QST may be observed as a strength of study. The third limitation is that we did not evaluate the patients' pre- and posttreatment analgesic consumption. Finally, we did not include patients with a history of psychiatric illness, but not evaluating the current psychiatric conditions of the patients can be considered a limitation. Nevertheless, the main strengths of this study are its prospective design and, to our knowledge, it is the first study to explore the effects of CS on cervical ESI treatment.

## Conclusions

The presence of CS has a negative effect on pain scores, disability, and quality of life in patients undergoing cervical ESI due to CDH. In this respect, the presence of CS should not be ignored while planning the treatment of patients who will receive cervical ESI injections.

## References


1. Cohen SP, Hooten WM. Advances in the diagnosis and management of neck pain. *BMJ* 2017; 358:j3221.
2. Sharrak S, Al Khalili Y (eds.). Cervical disc herniation. In: *StatPearls* [Internet]. StatPearls Publishing, Treasure Island, FL 2021 {AU: Update to 2022 edition?}.
3. Manchikanti L, Cash KA, Pampati V, et al. Management of chronic pain of cervical disc herniation and radiculitis with fluoroscopic cervical interlaminar epidural injections. *Int J Med Sci* 2012; 9:424-434.
4. McCormick Z, Plastaras C. Lumbosacral transforaminal epidural steroid injections are equally effective for treatment of lumbosacral radicular pain in the obese compared to non-obese population: A pilot study. *J Back Musculoskelet Rehabil* 2013; 26: 183-188.
5. den Boer C, Dries L, Terluin B, et al. Central sensitization in chronic pain and medically unexplained symptom research: A systematic review of definitions, operationalizations and measurement instruments. *J Psychosom Res* 2019; 117:32-40.
6. Pak DJ, Yong RJ, Kaye AD, et al. Chronification of pain: Mechanisms, current understanding, and clinical implications. *Curr Pain Headache Rep* 2018; 22:9.
7. Wylde V, Sayers A, Odutola A, et al. Central sensitization as a determinant of patients' benefit from total hip and knee replacement. *Eur J Pain* 2017; 21:357-365.
8. Bennett EE, Walsh KM, Thompson NR, et al. Central sensitization inventory as a predictor of worse quality of life measures and increased length of stay following spinal fusion. *World Neurosurg* 2017; 104:594-600.
9. Neblett R, Hartzell MM, Mayer TG, et al. Establishing clinically relevant severity levels for the central sensitization inventory. *Pain Pract* 2017; 17:166-175.
10. Schiff E, Eisenberg E. Can quantitative sensory testing predict the outcome of epidural steroid injections in sciatica? A preliminary study. *Anesth Analg* 2003; 97:828-832.
11. Shigetoh H, Koga M, Tanaka Y, et al. Central sensitivity is associated with poor recovery of pain: Prediction, cluster, and decision tree analyses. *Pain Research and Management* 2020; 2020:8844219.
12. Mehta V, Snidvongs S, Ghai B, et al. Characterization of peripheral and central sensitization after dorsal root ganglion intervention in patients with unilateral lumbosacral radicular pain: A prospective pilot study. *Br J Anaesth* 2017; 118:924-931.
13. Blozik E, Himmel W, Kochen MM, et al. Sensitivity to change of the neck pain and disability scale. *European Spine Journal* 2010; 20:882-889.
14. Bicer A, Yazici A, Camdeviren H, et al. Assessment of pain and disability in patients with chronic neck pain: Reliability and construct validity of the Turkish version of the neck pain and disability scale. *Disabil Rehabil* 2004; 26:959-962.
15. Bennett M. The LANSS pain scale: The Leeds assessment of neuropathic symptoms and signs. *Pain* 2001; 92:147-157.
16. Gandek B, Ware JE, Aaronson NK, et al. Cross-Validation of item selection and scoring for the SF-12 health survey in nine countries: Results from the IQOLA Project. International Quality of Life Assessment. *J Clin Epidemiol* 1998; 51:1171-1178.
17. Mayer TG, Neblett R, Cohen H, et al. The development and psychometric validation of the central sensitization inventory. *Pain Pract* 2012; 12:276-285.
18. Düzce Keleş E, Birtane M, Ekuklu G, et al. Validity and reliability of the Turkish version of the central sensitization inventory. *Arch Rheumatol* 2021:36: 518-526.
19. Latremoliere A, Woolf CJ. Central sensitization: A generator of pain hypersensitivity by central neural plasticity. *J Pain* 2009; 10:895-926.
20. Kondo Y, Miki T, Higuchi D, et al. Effects of central sensitivity syndrome and psychological factors on the clinical features of patients with cervical degenerative disease: A cross-sectional study. *Asian Spine J* 2021; 15:464-471.
21. House LM, Barrette K, Mattie R, et al. Cervical epidural steroid injection: Techniques and evidence. *Phys Med Rehabil Clin N Am* 2018; 29:1-17.
22. Sanal-Toprak C, Ozturk EC, Yucel FN, et al. Does the presence of neuropathic pain affect the outcomes of the interlaminar epidural steroid injection for cervical disc herniation?: A prospective clinical study. *Medicine (Baltimore)* 2021; 100:e25012.
23. Yoon JY, Kwon JW, Yoon YC, et al. Cervical interlaminar epidural steroid injection for unilateral cervical radiculopathy: Comparison of midline and paramedian approaches for efficacy. *Korean J Radiol* 2015; 16:604-612.
24. Cuéllar JM, Borges PM, Cuéllar VG, et al. Cytokine expression in the epidural space: A model of noncompressive disc herniation-induced inflammation. *Spine (Phila Pa 1976)* 2013; 38:17-23.
25. Neblett R, Hartzell MM, Williams M, et al. Use of the central sensitization inventory (CSI) as a treatment outcome measure for patients with chronic spinal pain disorder in a functional restoration program. *Spine J* 2017; 17:1819-1829.
26. Kim MS, Koh IJ, Lee SY, et al. Central sensitization is a risk factor for wound complications after primary total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2018; 26:3419-3428.
27. Ohashi Y, Fukushima K, Uchida K, et al. Adverse effects of higher preoperative pain at rest, a central sensitization-related symptom, on outcomes after total hip arthroplasty in patients with osteoarthritis. *J Pain Res* 2021; 14:3345-3352.
28. Akeda K, Yamada J, Takegami N, et al. Evaluation of central sensitization inventory in patients undergoing elective spine surgery in a multicenter study. *Global Spine J* 2021. [Epub ahead of print]
29. Institute of Medicine Committee on Pain, Disability, and Chronic Illness Behavior. In: Osterweis M, Kleinman A, Mechanic D (eds). *Pain and Disability: Clinical, Behavioral, and Public Policy Perspectives*. National Academies Press (US), Washington, DC 1987.
30. Koh IJ, Kang BM, Kim MS, et al. How does preoperative central sensitization affect quality of life following total knee arthroplasty? *The Journal of Arthroplasty* 2020; 35:2044-2049.