Chronic outcomes of chronic radicular lumbosacral pain following epidural triamcinolone injection

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ABSTRACT

Introduction: Chronic radicular lumbosacral pain or CRLP is a unilateral or bilateral subjective sensation in the median or paramedian lumbar and/or sacral area radiating down to the leg of the involved nerve roots. Lately, it has been treated using epidural triamcinolone injection, but has limited measurement in pain scale and degree of disability. HMGB-1 has been considered to have a significant role in the chronicity of LBP. This study aims to determine changes in levels of the inflammatory biomarker HMGB-1 associated with clinical outcomes of CRLP after epidural triamcinolone injection.

Methods: This was an experimental study using a single-blind randomized control trial design, measuring changes in the degree of pain and disability using the pain scale and the Oswestry disability index (ODI) and analyzing HMGB-1 protein levels. Serum HMGB-1 was analyzed using the ELISA method. 57 participants were involved in the study and were divided randomly into 2 groups. Normalization of data distribution was tested using the Kolomogorov-Smirnov test; the outcome in each group were tested using the independent T-test and comparison of changes was tested using the Mann-Whitney U test. The correlation direction and strength between clinical outcomes and biomarker levels were tested using the ANOVA and multiple linear regression.

Results: The measurements of HMGB-1 protein levels before and after intervention in patients with CRLP pain showed a significant decrease in serum HMGB-1 on day 7 and was more significant in the intervention group. In comparative measurements of clinical outcomes measured by the pain scale and ODI before and after intervention, it was found that improvements in pain scales and disability scores were measured on the 7th day; this reduction was more significant in the intervention group.

Conclusion: There was an improvement in the clinical outcome after epidural triamcinolone administration was analyzed from serum HMGB-1 protein levels.

Keywords: chronic lumbosacral radicular pain, HMGB-1, epidural steroid injection, Oswestry disability index.

INTRODUCTION

Lumbosacral radicular pain is a unilateral or bilateral subjective and unpleasant sensation in the median or paramedian lumbar and/or sacral area radiating down to the leg according to the dermatomal distribution of the involved nerve roots for at least 3 months. The symptoms are experienced as a feeling of burning, tingling, or numbness accompanied by motor disturbances in the leg area if the pathological process involves motor nerves.1-3 Chronic lumbosacral radicular pain becomes important for three main reasons: the prevalence and incidence rate tend to increase; the high cost of burden disease; and the high recurrence rate.1-6 The Global Burden of Disease of Low Back Pain study shows that low back pain remains the main cause of disability worldwide. Global prevalence is higher in women than in men and increases with age, peaking in the 80–84 age group in both gender groups in 2019.7

Chronic lumbosacral radicular pain is a mixed pain of nociceptive and neuropathic pain.6 Nociceptive pain is characterized by sharp, localized pain, while neuropathic pain is characterized by hyperalgesia and allodynia due to peripheral and central sensitization. To measure changes in the degree of pain and disability, the pain scale and the Oswestry disability index (ODI) are usually used as measurement standards.

The etiologies of lumbosacral radicular pain vary from mechanical to nerve entrapment and tissue damage, which are converging in the inflammatory process. The inflammatory cascade is characterized by an increase in inflammatory markers such as IL, TNF-a, INF, NGF, and HMGB-1.8,9 This occurs due to annular tears and leakage of the nucleus pulposus matrix, most often by HNP into the epidural and foraminal spaces, triggering inflammation in the nerve roots and dorsal nerve root...
ganglion, the formation of fibrotic and granulation tissue in the epidural and foraminal spaces, inhibiting nerve root mobility, and entrapment in the foramen sub-compartment, which triggers pain. Confirmation of HNP lumbosacral radicular pain is by supine straight leg raise (lasegue test), which increases pain and MRI imaging examinations.

High Mobility Group Box-1 (HMGB-1) is a DNA-binding protein in the nucleus of mammalian cells, contributing to the structure of DNA chromatin, playing an important role in transcriptional activity in the cell nucleus, and as an intracellular messenger molecule, released from certain cells to the extracellular to have an effect on receptors certain cells. It has a molecular weight of 25 kDa of 215 amino acids with two domains for DNA binding, known as box A and box B, as well as a C-terminal acidic tail consisting of acidic residues formed by 30 glutamic acid and aspartic acid. repeating, and the remaining 20% is lysine.

The first proinflammatory barrier that is activated by the body's immune system is the release of HMGB-1 as a molecular pattern that is activated by tissue damage (damage-activated molecular pattern, or DAMP). This response can be acute or chronic. In an acute inflammatory response, tissue damage causes the release of HMGB-1 from cytoplasmic vesicles and plays an important role in the prolongation of the inflammatory process and the persistence of pain in chronic pain. The contribution of HMGB-1 to pain is associated with the activation of RAGE and TLR4 signaling primarily in spinal microglia and primary sensory neurons. TLRs receptors initiate intracellular signaling pathways, causing the synthesis and secretion of various inflammatory cytokines and chemokines, proving that TLRs and related signaling components contribute to pain hypersensitivity, and blockade of TLR signaling has been shown to reduce pathological pain. RAGE is found in the dorsal root ganglia (DRG) and involves oxidative stress, caspase activation, and pain chronization. A study of the relationship between RAGE and pain found that the RAGE-NF-κB axis acts on the deficit of exacerbating functional sensory deficits in diabetic neuropathy. RAGE interaction induces oxidative stress to increase the thermal nociceptive threshold in a diabetes model, making it interesting to assess the relationship between HMGB-1 and pain.

Chronization and recurrence of lumbosacral radicular pain are associated with failure to treat the acute phase of pain. Epidural steroid injection intervention has recently become an option for treating chronic lumbosacral radicular pain for several reasons, namely: selective infiltration of the structures that cause pain with local anesthesia reduces the patient's typical pain by temporarily blocking the activity of stimulated nociceptors; stimulation of nociceptors associated with inflammatory processes such as phospholipase A2 can be inhibited by locally delivered steroid deposits, with resulting therapeutic benefits.

Triamcinolone is more often used for epidural injection in the lumbosacral segment for spinal pain because of its long-acting effect (32–72 hours) compared to other classes of injectable steroids. Injection of triamcinolone into the epidural space can reduce nociceptive signals from irritated nerve roots by inhibiting the formation and release of inflammatory cytokines, stabilizing nerve membranes, and modulating peripheral nociceptive pathways. However, no studies have directly examined the relationship between HMGB-1, pain scales, and clinical outcomes after administration of triamcinolone. Therefore, this study aims to determine changes in levels of the inflammatory biomarker HMGB-1 associated with clinical outcomes of CRLP after epidural triamcinolone injection.

**METHODS**

This was an experimental study using a single-blind randomized control trial design, measuring changes in the degree of pain and disability using the pain scale and the Oswestry disability index (ODI) and analyzing HMGB-1 protein levels. Serum HMGB-1 was analyzed using the ELISA method. A total of 57 participants were involved in the study and were divided randomly into 2 groups: the intervention group (conservative therapy and epidural triamcinolone injection intervention; n = 37) and the control group (only received 8 mg of dexamethasone sodium phosphate; n = 20). Inclusion criteria include: a sample age of 18–70 years; pain in the lumbosacral area radiating down to the pelvis and legs for at least 12 weeks; patients with intervertebral disc disorders with symptoms of pain in the lumbosacral area that are felt to radiate to the pelvis and legs for at least 12 weeks; and mild spinal stenosis. Exclusion criteria include lower back pain with clinical symptoms related to facet joint impairment; history of lower back surgery; history of active malignancy less than 2 years; history of spinal fracture in the pelvic or lumbar region for less than 12 months; locus of active infection in the body; coagulation disorders and being on current anticoagulant therapy, excluding aspirin; chronic treatment with NSAIDs; receiving a steroid injection less than 2 weeks apart for back pain or other pathology; and history of active autoimmune disease or inflammatory arthritis. The drop-out criteria is that patients were absent for blood sampling or did not complete the entire series of blood samplings.

**Data collection**

Patients who met the diagnostic and inclusion criteria received verbal and written explanations regarding the research and were asked to sign informed consent. Anamnesis, straight leg raising (SLR) tests, and pain scale assessments were carried out by doctors at the Neurology ward who did not know about the research plan. The pain scale and ODI assessment were carried out by a professional physiotherapist, who also did not inform about the research. The pain scale was assessed three times: baseline before intervention, NPRS I, which was assessed 24 hours after the intervention, and NPRS II, 7 days after the intervention. The diagnosis of chronic lumbosacral radicular pain was established if the SLR test was positive and confirmed by T2WI MRI imaging, which shows a picture of the high-intensity zone (HIZ), bulging, or protrusion of lumbar discs.

The Numeric Pain Rating Scale (NPRS) is an outcome measure that is a unidimensional measure of pain intensity in adults, in which a respondent selects a whole number (0–10 integers) that best
reflects the intensity of his or her pain, from ‘0’ representing no pain to ‘10’ representing the most severe pain.

The Oswestry Disability Index (ODI) is a patient-completed questionnaire that gives a subjective percentage score of level of function in activities of daily living for those rehabilitating from low back pain, including pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex, social, and travel. Each item consists of six statements that are scored from 0 to 5, with 0 indicating the least disability and 5 the greatest. The total score is then calculated as a percentage, with 0% indicating no disability and 100% disability.

**Human Mobility Group Box-1 (HMGB-1)** is a DNA-binding protein in the nucleus of mammalian cells, contributing to the structure of DNA chromatin and playing an important role in transcriptional activity in the cell nucleus. As an intracellular messenger molecule, it is released from certain cells to the extracellular to have an effect on receptors in certain cells. The first proinflammatory barrier that is activated by the body's immune system is the release of HMGB-1 as a molecular pattern that is activated by tissue damage (damage-activated molecular pattern, or DAMP). It has a molecular weight of 25 kDa of 215 amino acids with two domains for DNA binding, known as box A and box B, as well as a C-terminal acidic tail consisting of acidic residues formed by 30 glutamic acid and aspartic acid. repeating, and the remaining 20% is lysine.

**Blood sample preparations**

Blood sampling is carried out as part of screening criteria and baseline measurements. Outcome measurement was carried out three times, i.e., before the intervention, 24 hours later, and 1 week after the intervention.

**Human Mobility Group Box 1 (HMGB-1).** HMGB-1 protein levels were measured by taking 3 ml of venous blood samples three times: before the intervention, 24 hours later, and 9 days after the intervention, using the ELISA method. A total of 3 ml of venous blood was taken with the EDTA-Na2 anticoagulant. Store for 30 minutes at room temperature, and then centrifuge for 15 minutes at a speed of 1000 x g at a temperature of 2–8 degrees Celsius. The plasma supernatant formed on the surface of the tube was collected for assay preparation. Human HMGB-1 (High Mobility Group Protein B1) from Elabscience™ with catalog number E-EL-H1554 and product size 96T.

**Reagent dilution:** Two stages of reagent dilution of 1000-fold were carried out as follows: 5 µL of sample was added to 95 µL of dilution solution to obtain a 20-fold dilution. Next, add 5 µL of the 20-fold dilution solution to 245 µL of the dilution solution to obtain a 1000-fold dilution.

**Assay procedure:** All diluted materials (dilution standards, blank participants, and antigen) were prepared. The plate was prepared with specific antibodies (non-specific binding sites are blocked). 100 µL of each ingredient was inserted into the specified plate, then the plate was covered with the prepared lid and incubated for 90 minutes at 37 degrees Celsius. Next, the plate was removed from the incubator and the excess liquid was discarded. Immediately, 100 µL of biotinylated detection Ab solution was added to each hole, and the plate was covered again with a new cover that had been prepared. The plate was incubated for 60 minutes at 37 degrees Celsius. The plate was washed three times to remove excess unreacted antigen. 100 µL of primary antibody was added to specifically bind to the HMGB-1 antigen. Then secondary antibodies labeled with enzymes were added to bind to the primary antibodies, and the plate was again incubated for 30 minutes at 37 degrees Celsius. The plate was washed five times to remove unbound antibody-enzyme conjugates. Finally, 90 µL of substrate reagent was added to the plate to be converted by the enzyme into a precipitated color, and the color intensity was measured. Cover the plate with a new lid that has been prepared, protect it from direct sunlight, and then incubate for 15 minutes at a temperature of 37 degrees Celsius. Added 50 µL of stop solution to stop the reaction. Color intensity was measured using a reader/ spectrophotometer at a wavelength of 450nm using Elisa.

**Dexamethasone injection.**

1) The patient was laid in a prone position on the procedure table; 2) the skin around the lumbar sacrum was prepared steriley using povidone-iodine (Betadine) followed by an alcohol rinse; 3) the target area or spinal location to be injected was identified and the desired needle path was determined using the C-Arm tool with fluoroscopy; 4) patients received the allocated steroid preparations as a 2 ml solution; 5) patients received 8 mg of dexamethasone sodium phosphate; 6) control epidurogram after the transforaminal lumbar epidural injection procedure was confirmed to ensure the interventional procedure was completed without new neurological deficits.

**Transforaminal epidural triamcinolone injection**

Intervention Method for Epidural Triamcinolone Injection with Transforaminal Technique According to International Standards: 1) The patient was laid in a prone position on the procedure table; 2) the skin around the lumbar sacrum was prepared steriley using povidone-iodine (Betadine) followed by an alcohol rinse; 3) the target area or spinal location to be injected was identified and the desired needle path was determined using the C-Arm tool with fluoroscopy; 4) the best ipsilateral oblique view of the lumbar spine for targeted transforaminal lumbar epidural injection was identified; 5) Local anesthesia with 2% Lidocaine was injected at the intended site for epidural needle insertion; 6) A 23G-spinal needle was inserted into the intervertebral foramen targeted for epidural injection; 7) the needle tip with antero-posterior (AP) and lateral views in the epidural space was confirmed with contrast agent for AP and lateral fluoroscopy images; 8) Forty (40) mg of triamcinolone acetate with 1 cc of 1% lidocaine was injected transforaminal, followed by flushing 1 cc of normal saline into the transforaminal epidural space to target the inflamed spinal nerve roots caused by hernia nucleus pulposus (bulging disc protrusion) and mechanical adhesiolysis; 9) control epidurogram after the transforaminal lumbar epidural injection procedure was confirmed to ensure the interventional procedure was completed without new neurological deficits.
Statistical analysis
Normalization of data distribution was analyzed using the Kolmogorov-Smirnov test; the changes in clinical outcomes before and after intervention in each group were tested using an independent T-test; comparison of the changes between intervention and control groups was analyzed using the Mann-Whitney U test; and the direction and strength of the correlation between clinical outcomes and biomarker levels were analyzed using the ANOVA and multiple logistic regression.

RESULTS
A total of 60 patients met the inclusion criteria. Of this number, three (3) participants dropped out because they did not come for the second blood collection after the intervention. The characteristics and univariate analysis of the research participants are shown in Table 1. Univariate analysis determines the significant differences in the characteristics

Table 1. Characteristics and univariate analysis of research participants

<table>
<thead>
<tr>
<th>Characteristics (N=57)</th>
<th>Control (n=20)</th>
<th>Intervention (n=37)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>Sex (n; %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y.o; Mean±SD)</td>
<td>24</td>
<td>80</td>
<td>50.05 (±14.53)</td>
</tr>
<tr>
<td>Onset (month; Mean±SD)</td>
<td>3</td>
<td>18</td>
<td>11.46 (±4.78)</td>
</tr>
<tr>
<td>Pain area (f; %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>right</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>left</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Pain Scale</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Mean±SD)</td>
<td>4</td>
<td>8</td>
<td>5.58 (±1.06)</td>
</tr>
<tr>
<td>ODI Score (Mean±SD)</td>
<td>26</td>
<td>36</td>
<td>29 (±3.044)</td>
</tr>
<tr>
<td>HMGB-1 Baseline (pg/ml; Mean±SD)</td>
<td>3366.26</td>
<td>6220.76</td>
<td>4800.01 (±854.01)</td>
</tr>
</tbody>
</table>

Source: primary data
ODI: Oswestry disability index; HMGB-1: High mobility group box-1; pg: picogram

Figure 1. Flow chart of the study
of the two research groups, which could influence the research results. Table 1 reveals that the total number of research participants in both groups was 57 (26 male and 31 female). All 57 participants were randomly distributed in the intervention group (N = 37; male = 16; female = 21) and in the control group (N = 20; male = 10; female = 10), with no significant difference in gender distribution between the two groups (p-value = 0.625). The age of participants ranges from 22 to 70 years based on the inclusion criteria established, with the average age of the sample in the intervention group being 46.73 (± 15.59) and the control group being 50.09 (± 14.53) with a p-value of 0.436. The pain characteristics in the intervention group include: the mean pain onset was 5.54 (±1.135); the average pain onset was >3 months with a mean value of 9.60 (±5.807); the radiated pain is dominantly unilateral (right n = 22; left n = 14; bilateral n = 1); and the mean disability score was 28.81 (± 2.663). Meanwhile, in the control group, the mean pain scale was 5.58 (±1.056), the mean pain onset was 11.46 months (±4.776), the radicular pain was predominantly unilateral (right n = 11; left n = 9), and the mean disability score was 29.0 (± 3.044). The p-values for all pain characteristics show significant differences between the two groups in Table 1. The mean measurement of baseline HMGB-1 in the intervention group was 4698.72 pg/mL (±813.043) pg/mL, compared to that in the control group, which was 4748.48 pg/mL (± 854,011). The univariate analysis shows no significant difference in the mean baseline HMGB-1 in the two study groups, with a p-value of 0.709.

One objective of this study was to assess changes in pain scale and disability score between the groups after epidural triamcinolone injection. The average NPRS value can be seen in Table 2. In general, a significant change in the mean pain scale after epidural triamcinolone injection, where the improvement in the pain scale was found to be greater in the intervention group than in the control group.

In disability score, a significant change in the mean ODI score was also seen in the ODI II measurement after 7 days of intervention for 18.76 (± 3.34) in the intervention group and 23.30 (± 2.49) in the control group with a p-value < 0.05 when compared with the significance of changes in ODI scores after 24 hours of intervention with a p-value = 0.369 (Table 2). The significance of changes in disability scores between groups was carried out by comparing delta changes in baseline ODI and ODI II using the Mann-Whitney U test, which shows a p-value of 0.01 (Table 3). This means that there is a significant difference in the improvement in ODI scores after the epidural triamcinolone injection intervention, where the improvement in scores is greater in the intervention group than in the control group.

The average HMGB-1 protein levels are shown in Table 2. A significant change in the mean HMGB-1 protein level was seen in HMGB-1 II measurements after 7 days of intervention, which are 4578.214 pg/mL (± 1215.181) and 5238.461 pg/mL (± 208) in the intervention and control groups, respectively (p-value = 0.043). The delta changes in baseline HMGB-1 and HMGB-1 II in each group show a p-value of 0.003 (Table 3), indicating a significant difference in HMGB-1 protein levels after epidural triamcinolone injection, where the changes are shown to be greater in intervention than in the control counterpart group.

**DISCUSSION**

Based on both groups, the characteristics of the subjects were dominated by the female gender. This is in accordance with the research of Wang et al., who examined the epidemiological trends of low back pain at the global, regional, and national levels, explaining that statistically, the

### Table 2. Changes in NPRS, ODI, and HMGB-1 in baseline, I, dan II measurements in intervention and control groups.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Intervention (n=37) Mean (±SD)</th>
<th>Control (n=37) Mean (±SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Scale (NPRS)</td>
<td>5.54 (± 1.33)</td>
<td>5.80 (± 1.06)</td>
<td>0.454</td>
</tr>
<tr>
<td>Baseline</td>
<td>4.81 (± 1.29)</td>
<td>4.85 (± 0.813)</td>
<td>0.902</td>
</tr>
<tr>
<td>Measurement I</td>
<td>3.43 (± 1.07)</td>
<td>4.60 (± 0.883)</td>
<td>0.010*</td>
</tr>
<tr>
<td>Measurement II</td>
<td>28.73 (± 3.12)</td>
<td>28.85 (± 3.18)</td>
<td>0.891</td>
</tr>
<tr>
<td>Disability (ODI)</td>
<td>27.95 (± 2.91)</td>
<td>28.70 (± 3.164)</td>
<td>0.369</td>
</tr>
<tr>
<td>Baseline</td>
<td>18.76 (± 3.34)</td>
<td>23.30 (± 2.49)</td>
<td>0.010*</td>
</tr>
<tr>
<td>Measurement I</td>
<td>4689.72 (± 813.04)</td>
<td>4800.01 (± 920.92)</td>
<td>0.643</td>
</tr>
<tr>
<td>Measurement II</td>
<td>4615.28 (±1058.08)</td>
<td>4854.26 (± 1027.60)</td>
<td>0.415</td>
</tr>
</tbody>
</table>

*significant at p<0.05 by independent t-test; SD = standard of deviation

### Table 3. Comparison of NPRS, ODI, and HMGB-1 changes in control and intervention groups before and after epidural triamcinolone injection

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Intervention (n=37) Mean (±SD)</th>
<th>Control (n=37) Mean (±SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ NPRS</td>
<td>2.11 (±1.39)</td>
<td>1.10 (±0.85)</td>
<td>0.050*</td>
</tr>
<tr>
<td>Δ ODI</td>
<td>9.68 (±1.87)</td>
<td>5.60 (±1.82)</td>
<td>0.010*</td>
</tr>
<tr>
<td>Δ HMGB-1</td>
<td>-111.51 (±1232.93)</td>
<td>438.45 (±711.03)</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

*significant at p<0.05 by independent t-test; SD = standard of deviation; Δ, changes

**ORIGINAL ARTICLE**

high life expectancy of women influences the large number of female patients who experience low back pain. In addition, women work with a higher intensity of housework in non-ergonomic positions, more overload of the back due to anatomical and functional differences with men, and pregnancy-related physiological alterations.15

Furthermore, the average age characteristics of the subjects in this study were 46 years. This was also mentioned in research by Wang et al., who explained that population aging is expected to dramatically increase the economic and healthcare burdens due to musculoskeletal (MSK) conditions in the future, such as LBP, and that its increasing disease burden is largely associated with population aging.15 According to data from the GBD 2019 study, the age-standardized incidence rate was mostly observed in the 80–84 age group. In addition, the largest number of people with LBP globally are in the 50–54 age group. In addition, the greatest number of people with LBP globally are in the 50–54 group.16

A recent low back pain study demonstrated the involvement of the sterile inflammatory biomarker HMGB-1 in the pathophysiology of non-specific low back pain. The current study aims to measure changes in HMGB-1 and NGF levels after epidural triamcinolone injection intervention in patients with chronic lumbosacral radicular pain and their effect on the degree of pain and disability, involving 57 research samples with an average age of 50 years. Demographic data related to age in the incidence of chronic lumbosacral radicular pain is in line with data on demographic characteristics in previous research, which states that age is a primary factor for LBP associated with degenerative processes, where the highest prevalence is found in the 4th–5th decade age group.17

The definition of lumbosacral radicular pain in this study refers to IASP 1994, which states that pain radiates down to the leg due to spinal nerve root dysfunction. The diagnosis of lumbosacral radicular pain in this study was confirmed by anamnesis in the form of complaints of pain in the lumbosacral area that radiated to the legs, both unilaterally and bilaterally; confirmed by the Lasegue test; and supported by the results of a lumbosacral MRI examination if it shows a disc herniation or mild spinal canal stenosis. A review study from Cochrane stated that the clinical picture of chronic lumbosacral radicular pain is dominated by pain in the lumbar region, with pain spreading only to the area below the knee, and/or other clinical pictures in the form of unilateral or bilateral leg pain, in line with the clinical picture in the sample of this research.18 This review study also states that the diagnosis of lumbosacral radicular pain can be made either by clinical assessment and radiological examination or only based on the results of the clinical assessment alone.19

Triamcinolone injections into the epidural space also function as a lavage of the epidural space and lyse epidural adhesions and nerve roots. In one systematic review, there was a strong correlation between epidural injection volume and outcome, regardless of steroid dose.19 In another systematic review and meta-analysis evaluating control group effects in randomized controlled trials, Freeman et al. found that epidural nonsteroidal injections, such as transforaminal epidural etanercept injection, provided greater benefit than non epidural injections, such as placebo.20

A prospective, randomized, single-blind study was conducted comparing the clinical efficacy of transforaminal epidural injections of dexamethasone and triamcinolone in the management of chronic lumbosacral radicular pain in eighty patients with and without radiculopathy due to intervertebral disc herniation. In this study, the patients were divided into two groups: those receiving an 8 mg dexamethasone injection or those receiving a 40 mg triamcinolone acetonide injection via the transforaminal epidural route. Each patient underwent a unilateral transforaminal lumbar epidural steroid injection (TFESI) into the involved nerve root segment, and spinal magnetic resonance imaging computed tomography demonstrated results consistent with the patient's clinical presentation. Patients in both groups were assessed for pain intensity before epidural injection and at 2, 6, and 12 weeks after epidural injection and weekly analgesic requirements. This study showed significantly better changes in pain scores with transforaminal epidural injection of triamcinolone acetonide compared with dexamethasone in patients with chronic lumbosacral radicular pain due to intervertebral disc herniation.14

In the current study, changes in pain scales and ODI scores were assessed before and after epidural triamcinolone injection intervention. The pain scale and ODI score are two clinical outcome parameters commonly used to assess the success of epidural therapeutic agent injection interventions.21

The results in Tables 2 and 3 show that there are significant differences in NPRS and ODI scores between the control and intervention groups on the 7th day after the intervention. The values were also significantly different when compared with baseline values. This is in accordance with research by Sahu et al., which obtained the same value and stated that radicular pain is the product of both compression of neural tissue and an inflammatory response; tumor necrosis factor α, phospholipase A2, interleukins 1 and 6, and nitric oxide have been implicated in the inflammatory response. When the inflammatory component dominates, patients may be more responsive to transforaminal epidural steroid injections than in highly compressive lesions. These factors will not influence the immediate anesthetic block; patients will gain much more strongly associated with longer-term outcomes in response to the anesthetic blockade.14

Another study by Imani et al., which examined the comparison of transforaminal triamcinolone and dexmedetomidine in radicular low-back pain, showed the same significant results on VAS and ODI. Imani stated that transforaminal steroids not only have short-term analgesic effects lasting only for three months, but they also have little effect on physical disability and the incidence of subsequent surgical procedures.22 In another study, Kim et al. reported that the administration of triamcinolone was associated with higher efficacy and satisfaction than the administration of epidural dexamethasone.23

In our study, a comparison of the significance of changes in HMGB-1
protein levels between the intervention and control groups was assessed. This was performed by comparing the delta changes in baseline HMGB1 and HMGB-1 II protein levels in each group using the nonparametric Man-Whitney U test. The results of this comparison test showed a p-value of 0.03, which means there is a significant difference between HMGB-1 protein levels after epidural triamcinolone injection intervention, where the change in levels was greater in the intervention group than in the control group.

One study measured serum triamcinolone levels after epidural injection to investigate the pharmacokinetics of epidurally administered triamcinolone acetonide under fluoroscopic guidance in a group of patients with chronic lumbosacral radicular pain. The final elimination half-life of triamcinolone after epidural injection in noncompartmental analysis was 523 hours, or the equivalent up periods are needed to confirm the findings of this study.

CONCLUSION
The measurements of HMGB-1 protein levels before and after epidural triamcinolone intervention in patients with chronic lumbosacral radicular pain showed a significant decrease in serum HMGB-1 on day 7 after epidural triamcinolone injection compared to the conventional treatment. Since the follow-up time was only 7 days, multicenter trials with large sample sizes and longer follow-up periods are needed to confirm the findings of this study.

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