Predictive factors for treatment success of transforaminal epidural steroid injection in lumbar disc herniation-induced sciatica

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Running Head: Success of transforaminal epidural steroid injection

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ABSTRACT

Background: The aim of this study was to identify predictive factors for treatment success of transforaminal epidural steroid injection in patients with lumbar disc herniation-induced sciatica.

Materials and methods: A total of 219 patients who were diagnosed with unilateral sciatica and underwent transforaminal epidural steroid injection at the level of L4-5, L5-S1 or S1 neural foramina between March 2016 and May 2018 were retrospectively analyzed. The presence of transitional vertebrae and the grade of nerve root compression were evaluated by a radiologist. Data including age, sex, body mass index, duration of symptoms, injection levels and pain scores recorded. Pain scores were evaluated using the Numerical Rating Scale. Treatment success was defined as a ≥50% decrease in the pain scores at three months.

RESULTS: Of the patients 118 were females and 101 were males with a mean age of 43.65±12.18 years. The mean duration of symptoms was 25.64±2.17 weeks. Although the duration of symptoms was longer in patients in whom treatment failed, it did not reach statistical significance. Decreased pain scores at one hour had a significant effect on the treatment success (p=0.012, OR: 1.015 95% CI, 1.003-1.026).

CONCLUSIONS: Our study results suggest that decreased pain scores at one hour are predictors for a favorable three-month response to transforaminal epidural steroid injection in patients with lumbar disc herniation-induced sciatica.

KEYWORDS: Epidural injection, herniated disc, low back pain, back pain with radiation, magnetic resonance imaging, sciatica.
1. Introduction

Lumbar disc herniation (LDH)-induced sciatica is a common health problem with a lifelong prevalence of 12.2 to 43% and an annual prevalence of 2.2 to 34% (1). Pain is triggered by mechanical compression on the dorsal root or ganglion of the herniated disc material or inflammation induced by chemokines and enzymes in the disc (2). Several studies have shown the short-term efficacy of transforaminal epidural steroid injection (TFESI), which is commonly used in clinical practice, in the treatment of sciatica (3, 4). It has been proposed that it exerts its effect through the anti-inflammatory and neural membrane stabilization effect of the steroid injection, increased blood flow of the ischemic spinal root by the local anesthetic agent, and removal of cytokines due to the washout effect of the injection material (5, 6). In addition, TFESI is target-specific and is a favorable option to deliver the injection material to the ventral epidural site where pathological alterations occur (7).

Despite established short-term efficacy of TFESI in the treatment of LDH-induced sciatica, similar treatment outcomes may not be obtained in all patients. This indicates that there are several factors which affect the treatment success. Thus, a number of studies have been carried out investigating clinical and radiological parameters which can affect the TFESI outcomes (8-21). These studies have shown that duration of symptoms before TFESI has an effect on the treatment outcomes with an inverse correlation between duration of pre-treatment symptoms and treatment outcomes (11, 16, 21). In addition, some authors have demonstrated that duration of symptoms has no effect on the treatment outcomes (10, 18). Also, spinal nerve root compression as assessed by lumbar magnetic resonance imaging (MRI) has been found to be associated with decreased pain scores after TFESI and low-grade nerve root compressions better respond to the treatment (9, 10). In contrast, some authors advocated that high-grade spinal nerve compression positively affect the treatment response or there is no correlation between the grade of the nerve root compression and treatment outcomes (12, 13).
To the best of our knowledge, there is a limited number of study investigating possible factors affecting the treatment outcomes in the literature. Therefore, the role of clinical and radiological parameters on TFESI outcomes still remains to be elucidated and the predictive factors for treatment success are not clearly understood. In the present study, we aimed to identify predictive factors for treatment success of TFESI in patients with LDH-induced sciatica.

2. Materials and methods

All patients who were diagnosed with LDH-induced sciatica as confirmed by physical examination and lumbar MRI and underwent TFESI at standard doses of corticosteroids and local anesthetics between March 2016 and May 2018 were retrospectively analyzed. Of 826 patients who underwent TFESI, 219 who met the inclusion criteria were included in the study. Inclusion criteria were as follows: 18 to 65 years of age; LDH at the level of L3-4, L4-5 or L5-S1 as evidenced by MRI and TFESI due to unilateral L4, L5 or S1 spinal nerve root compression; and complete three-month follow-up data. Exclusion criteria were as follows: prior lumbar surgery including lumbar fusion or laminectomy; lumbar spinal stenosis, spondylosis, or spondylolisthesis; local or systemic infections; inflammatory rheumatic diseases such as ankylosing spondylitis, psoriatic arthritis; history of malignancy; repeated TFESI during <3-month follow-up or missing data.

Data including age, sex, body mass index (BMI), duration of symptoms, and injection levels were recorded. Pain scores were evaluated before and at one hour, three weeks, and three months after TFESI using the Numerical Rating Scale (NRS). The presence of transitional vertebrae and the grade of nerve root compression were evaluated by a radiologist. Treatment success was defined as a ≥50% decrease in the pain scores at three months (22, 23). The study protocol was approved by the Ethics Committee of Marmara University, Faculty of Medicine (No. 09.2018.591). The study was conducted in accordance with the principles of the Declaration of Helsinki. As it is routine practice for transforaminal epidural steroid injection
procedures in our clinic, all patients were asked to fill out and sign the standard patient consent form prior to the procedure. The ethics committee waived the requirement for informed patient consent because no patient re-contact was established for this study.

2.1 Radiological Assessment

The radiologist who was blinded to all clinical data had seven years of experience in spinal and musculoskeletal imaging. Cervicothoracic sagittal scout images were accepted as the gold standard for numbering the lumbar vertebral segments (24). The vertebrae were numbered by counting caudally from C2 with cross-referencing cervicothoracic and lumbar sagittal MRI scans on the Picture Archiving and Communication System (PACS) (Carestream Health Inc., Rochester, NY, USA) workstation using spinal-tagging properties of the software. The presence of lumbar transitional vertebrae was recorded according to the vertebra count and numbering.

The grade of nerve compression was assessed on axial T2-weighted images and sagittal T1-weighted images, respectively. In classification of spinal nerve root compression, the modified Pfirrmann grading system was used for central and subarticular disc herniation (25). Accordingly, Grade I applies when the disc simply contacts the nerve root, Grade II when the nerve root is displaced, but with preservation of periradicular cerebrospinal fluid (CSF) or fat, Grade III when the periradicular CSF or fat is obliterated, and Grade IV when the nerve root is morphologically distorted. Grade I-II indicates low-grade nerve root compression, while Grade III-IV indicates high-grade nerve root compression. No grading for foraminal herniation was used, due to the lack of data for foraminal and extraforaminal LDH patients.

TFESI Procedure

All patients were placed in the prone position and supported with a pillow under the abdomen to reduce lumbar lordosis. The injection site was cleaned up with povidone-iodine antiseptic three times and covered with a sterile dressing. The arm of the fluoroscopy was
rotated obliquely by 10 to 30 degrees toward the region in the cranial direction and the foramen was visualized. Local anesthesia (3 cc 2% prilocaine) was given to the skin and subcutaneous tissue. A Quincke 3.5-inch 22-gauge spinal needle was inserted under the intermittent guidance of fluoroscopy using coaxial technique and advanced to the subpedicular space in the 6 o’clock direction. The needle position was confirmed through a lateral view. Following confirmation, 1 to 2 mL contrast dye was given the needle position in the epidural space was confirmed in anteroposterior and lateral views. Once adequate flow of contrast dye was achieved without vascular flow, a mixture of 80 mg methyl prednisolone acetate, 1 cc physiological saline, and 1 cc (0.5%) bupivacaine was injected. And there were no acute complications after the TFESI in this study.

2.2 Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows version 24.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± SEM (standard error of measurement), number and frequency. The normality of distribution of continuous variables was tested using the Shapiro-Wilk test. The Mann-Whitney U test was used to compare two independent groups with abnormally distributed data. The chi-square test was applied to analyze the relationship between two categorical variables. Multivariate logistic regression analysis was performed to estimate the odds ratio (OR) and 95% confidence interval (CI). Univariate and multivariate regression analyses were carried out to identify possible predictive factors included age, sex, symptom duration, BMI, injection level, the presence of transitional vertebrae, NRS scores before injections, the grade of nerve root compression, post-procedural 1 hour NRS scores decrement for treatment success. A p value of <0.05 was considered statistically significant.

3. Results
Of the patients, 118 were females and 101 were males with a mean age of 43.65±12.18 years. The mean duration of symptoms before injection was 25.64±2.17 weeks. The most common nerve roots injected were L5 in 50.2%, S1 in 47.5%, and L4 in 2.3% patients. Demographic, radiological, and procedural characteristics are shown in Table 1.

Of the 219 patients who underwent TFESI, 124 (56.6%) were achieved treatment success at the 3rd month. There was no significant difference in the age, sex, BMI, injection level, the presence of transitional vertebrae, NRS scores before injections and the grade of nerve root compression between the patients with and without treatment success (Table 2, Table 3). Although the duration of symptoms was longer in patients in whom treatment failed, it remained at borderline significance (p=0.051). There was a higher decrease in pain scores at post-procedural one hour using NRS in patients in whom treatment was successful (p=0.024). Factors with a p value less than 0.10 in the univariate analysis were included in the multivariate binary logistic regression analysis. At the end of the analysis, duration of symptoms was not found to be a significant predictor for treatment success (p=0.391). Decreased pain scores at one hour had a significant effect on the treatment success (p=0.012, OR: 1.015 95% CI, 1.003-1.026) (Figure 1).

4. Discussion

With the introduction of spinal interventional pain management modalities in recent years, the number of pain interventionalists has been on a rise with a considerably increased treatment cost (26). Therefore, it is of utmost importance for clinicians to identify eligible patients in whom TFESI would be successful. Hence, predictive factors which affect the treatment outcomes positively or negatively should be established. In the present study, we evaluated predictive factors for treatment success of TFESI in patients with LDH-induced sciatica.
Among all parameters, only decreased pain scores at post-procedural one hour were found to be highly correlated with treatment success at three months.

In a study, Inman et al. (8) evaluated the effect of epidural steroid injection on pain in patients with low back pain and reported that sex was not a predictor for decreased pain scores. This finding is also consistent with our study which showed that sex had no effect on the treatment outcomes. In addition, this finding has been supported by several studies in the literature (9, 13, 14, 18). In our study, age was not a predictor for treatment success, either. This may be due to the fact that we excluded elderly patients with degenerative pathologies such as lumbar spinal stenosis or spondylosis and only included those with LDH-induced sciatica. This finding is supported in many studies in the literature (9, 11, 14, 18). In contrast, Lee et al. (13) showed that the mean age was higher in the patients in whom TFESI was successful, suggesting that young patients tended to have more components of nucleus pulposus, leading to inflammatory reaction and more resistant sciatica. However, these are short-term results. In another study, Ekedahl et al. (21) reported that young age was a strong predictor for one-year treatment response to TFESI, while BMI was not a predictive factor for three-month and one-year treatment response. To the best of our knowledge, there is scarce literature regarding the effect of BMI on the TFESI outcomes. In our study, we were also unable to identify BMI as a predictor for treatment outcomes during a three-month follow-up. This can be attributed to the small sample size in both studies.

In the present study, we applied the TFESI mostly at the level of L4-5, followed by the S1 foramen and L3-4 level. The injection level was not found to be a predictor for treatment outcomes. This finding is consistent with our clinical observations. However, six patients underwent TFESI at the level of L3-4. Although further large-scale studies are needed to obtain more accurate data, we conclude that our findings are consistent with the literature data (9, 18).

In their study, Son et al. (27) examined the effect of the presence of lumbar transitional
vertebrae on the treatment response to TFESI and reported that the presence of sacralized vertebrae had an adverse effect on treatment outcomes. In the aforementioned study, the authors found sacralization in 33 of 291 LDH patients. In our study, we also found sacralization in 18 of 219 patients. However, the lack of an effect of transitional vertebrae on treatment outcomes may be explained by the small sample size or the type of transitional vertebrae.

Spinal nerve root compression as assessed by lumbar MRI has been shown to be associated with decreased pain scores after TFESI and low-grade nerve root compressions better respond to the treatment (9, 10). In addition, some authors have suggested that patients with high-grade spinal nerve root compression respond to treatment better (12, 17). In a retrospective study, Paidin et al. (12) reported that higher resorption rates in patients with large disc herniation were associated with more favorable treatment response in patients with high-grade spinal nerve root compression. In addition, Ekedahl et al. (21) found that high-grade nerve root compression was a strong predictor for adverse treatment outcomes during one-year follow-up. On the other hand, consistent with our study findings, some authors have suggested that there is no correlation between spinal nerve root compression and treatment response (13, 19). In our study, we included patients with subarticular/central herniation and excluded those with foraminal herniation and, therefore, foraminal compression was unable to be evaluated. Further multi-center, large-scale, prospective studies are required to establish a definite conclusion.

In the present study, duration of symptoms was longer in patients in whom treatment was successful, indicating borderline significance. However, regression analysis revealed that it was not a predictor for treatment success. This finding is consistent with previous studies showing no correlation between the duration of symptoms and treatment outcomes (10, 18). However, several studies demonstrated that prolonged duration of symptoms adversely affected the treatment response (11, 21, 22). The discrepancy among the studies may be caused by the different sample sizes. In our study, decreased pain scores at post-procedural one hour were
highly correlated with the treatment success, indicating that more decrease in the pain scores may increase the chance of treatment success. In their study, El-Yahchouchi et al. (15) reported that immediate post-TFESI relief of index pain at two weeks was weakly associated with longer term outcomes of pain relief or functional recovery. This can be explained by the use of a different definition of treatment success and short-term follow-up results.

Only pain scores at post-procedural one hour which is a post-procedural factor were found highly correlated with the treatment success. Unfortunately, it is not pre-procedural factor. Therefore it will not contribute to predicting the success of treatment in patients before performing the procedure. On the other hand, this may be a chance for the patient and the clinician, because predicting treatment success at the first hour after the procedure (i.e in a short time after the procedure) seems to be valuable in giving the patient objective information about the treatment success of the procedure.

The main strength of our study is the inclusion of a homogeneous patient population with only LDH-induced sciatica and the ability of examining several clinical and radiological parameters. Nonetheless, the retrospective design with a short-term follow-up is the main limitation of this study. In addition, we were unable to analyze other factors such as contrast dispersal pattern in predicting treatment response.

5. Conclusion

Our study results suggest that decreased pain scores at one hour are predictors for a favorable three-month response to TFESI in patients with LDH-induced sciatica and can be used as a useful marker in identifying patients who would possibly to benefit from treatment. Nevertheless, further multi-center, large-scale, prospective studies are needed to elucidate possible predictive factors for treatment success.

6. Conflict of interest
The authors declare that they have no conflict of interest.

7. Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

Figure Legend

Figure 1. The relationship between decreased pain scores at post-procedural one hour and treatment success

Table Legends

Table 1. Demographic, radiological, and procedural characteristics

Table 2. Possible categorical variables

Table 3. Possible continuous variables
Table 1. Demographic, radiological, and procedural characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (n=219)</th>
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<tr>
<td>Age, mean ± SEM (years)</td>
<td>43.65±0.82</td>
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<td>Sex</td>
<td></td>
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<tr>
<td>Female</td>
<td>118 (53.9)</td>
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<tr>
<td>Male</td>
<td>111 (46.1)</td>
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<td>BMI, mean ± SEM (kg/m²)</td>
<td>27.06±0.29</td>
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<td>Mean duration of symptoms (weeks)</td>
<td>25.64±2.17</td>
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<tr>
<td>Level of injection</td>
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<tr>
<td>L4-5</td>
<td>5 (2.3)</td>
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<tr>
<td>L5-S1</td>
<td>110 (50.2)</td>
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<td>S1 foramen</td>
<td>104 (47.5)</td>
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<td>Nerve root compression (%)</td>
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<td>Grade 1</td>
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<td>Grade 2</td>
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<td>Grade 3</td>
<td>50 (23.9)</td>
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<td>Grade 4</td>
<td>60 (28.7)</td>
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<td>Transitional vertebrae</td>
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<td>Present (%)</td>
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<td>Absent (%)</td>
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<td>NRS, mean±SEM</td>
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<td>Before injection</td>
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<td>Post-procedural 1 h</td>
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<td>Week 3</td>
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<td>Month 3</td>
<td>3.84±0.20</td>
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BMI, body mass index; NRS: Numerical Rating Scale. Values expressed in mean ± SEM, number and frequency, or as otherwise indicated.
Table 2. Possible categorical variables

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<td>Sex</td>
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<tr>
<td>Female</td>
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<td>Male</td>
<td>54</td>
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<tr>
<td>Level of injection</td>
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<td>Absent</td>
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Table 3. Possible continuous variables

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<td>Age (years)</td>
<td>43.4 ± 1.14</td>
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<td>BMI</td>
<td>27.06 ± 0.39</td>
<td>27.06 ± 0.44</td>
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<td>Duration of Symptoms (weeks)</td>
<td>23.65 ± 2.84</td>
<td>28.24 ± 3.36</td>
<td>0.051</td>
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<td>NRS 1 hour decrements (%)</td>
<td>88.4 ± 1.89</td>
<td>79.5 ± 2.9</td>
<td><strong>0.024</strong></td>
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</tbody>
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NRS: Numerical rating scale, BMI: Body mass index
Figure 1. The relationship between decreased pain scores at post-procedural one hour and treatment success.