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The Impact of Hematological Parameters on Pain Relief After Transforaminal Epidural Steroid Injection

Hematolojik Parametrelerin Transforaminal Epidural Steroid Enjeksiyonu Sonrası Ağrı Azalması Üzerine Etkisi

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ABSTRACT

Objective: Since inflammation plays an important role in radiculopathies, and that neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratios (PLR) are known to be associated with inflammation, the effects of these values on transforaminal epidural steroid injections (TFESI) in patients with lumbar radiculopathy were investigated.

Methods: A total of 101 patients, who were diagnosed with lumbar radiculopathy and underwent TFESI, were retrospectively analyzed. Therapeutic success was considered to be a ≥ 50% decrease in visual analog scale (VAS) scores one month after TFESI. The patients in the study were placed in two groups according to whether their treatment was successful or unsuccessful, according to this criteria, and hemogram parameters in the two groups were then compared.

Results: The study included 46 female and 55 male patients with a mean age of 49.43 ± 13.29. The median duration of symptoms was 3.0 (3.0-8.0) months. It was found that there was no significant difference between the groups in terms of neutrophil, lymphocyte, monocyte, platelet counts, mean plazma volümü (MPV), kırmızı hücre dağılım genişliği (RDW), platelet/ lenfosit oranı (PLR), sistemik inflamatuar indeks (SII), sedimentation, and C-reactive protein (CRP), although it was observed that there were significant increases in NLR in the successful group [2.34 (1.70-3.17)], as compared to the unsuccessful group [1.79 (1.51-2.57)] (p=0.026).

Conclusion: Neutrophil/lymphocyte ratio is able to predict the response to TFESI treatment in patients with lumbar radiculopathy, in that patients with a higher NLR demonstrate a better response.

Keywords: Hemogram parameters, inflammation, neutrophil to lymphocyte ratio, lumbar disc herniation, lumbar radiculopathy

ÖZ

Amaç: Radikülopatilerde inflamasyon önemli rol oynadığından ve nötrofil/lenfosit oranı (NLO) ve trombosit/lenfosit oranlarının (TLO) inflamasyon ile ilişkileri bilindiğinden, bu değerlerin lomber radikülopatili hastalarda transforaminal epidural steroid enjeksiyonlarına (TFESİ) etkileri araştırıldı.

Yöntem: Lomber radikülopati tanısı alan ve TFESİ uygulanan toplam 101 hasta retrospektif olarak incelendi. Tedavi başarısı, TFESİ'den bir ay sonra vizüel analog skala (VAS) skorlarında ≥ %50 azalma olarak kabul edildi. Çalışmaya alınan hastalar TFESİ cevabına göre başarılı veya başarısız olarak iki gruba ayrıldı ve iki grup arasında hemogram parametreleri karşılaştırıldı.

Bulgular: Çalışmaya yaş ortalaması 49,43±13,29 olan 46 kadın ve 55 erkek hasta dahil edildi. Nötrofil, lenfosit, monosit, trombosit sayıları, mean plazma volümü (MPV), kırmızı hücre dağılım genişliği (RDW), platelet/ lenfosit oranı (PLR), sistemik inflamatuar indeks (SII), sedimantasyon ve C-reaktif protein (CRP) açısından gruplar arasında anlamlı fark saptanmadı. Nötrofil-lenfosit oranı başarılı grupta [2,34 (1,70-3,17)], başarısız gruba göre [1,79 (1,51-2,57)] istatistiksel olarak anlamlı derecede yüksek tespit edildi (p=0,026).

Sonuç: Nötrofil-lenfosit oranı, lomber radikülopatisi olan hastalarda TFESİ tedavisine yanıtı tahmin edebilir. Nötrofil lenfosit oranı yüksek hastalar TFESİ'ye daha iyi yanıt verirler.

Anahtar sözcükler: Hemogram parametreleri, inflamasyon, nötrofil lenfosit oranı, lomber disk herniasyonu, lomber radikülopati

INTRODUCTION

The most common cause of lumbar radiculopathy is lumbar disc herniation (LDH), the symptoms of which are normally lower back and leg pain. The prevalence of lumbar radiculopathy in the general population ranges from 2.2% to 8% (1). While the exact cause of pain due to LDH-induced radiculopathy is not fully understood, two possible theories have been proposed: mechanical compression and inflammation (2). Nucleus pulposus herniation, which is highly antigenic,

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causes inflammation by releasing numerous proinflammatory cytokines in the dura, nerve roots, and spinal cord (3). Although mechanical compression of a normal nerve usually does not cause pain, compression of an inflamed nerve normally does. In addition, inflammatory mediators have been experimentally shown to cause radicular pain in the absence of compression (2). This may explain the occurance of radicular symptoms and signs in some patients whom are not experiencing significant nerve root compression. It has therefore been concluded that mechanical compression is not the only cause of the pain experienced by patients.

Transforaminal epidural steroid injection (TFESI) is an effective treatment method commonly used in patients with lumbar radiculopathy which are normally unresponsive to conservative treatment (4). The injection of a mixture of steroids and local anesthetic into the epidural space not only has anti-inflammatory and neuronal membrane stabilization effect, it also increases blood flow in the ischemic spinal root (5,6). A systematic review has revealed the short-term efficacy of TFESI in lumbar radiculopathy (4).

Neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and systemic immune inflammation index (SII) are simple and practical markers of systemic inflammatory response that have recently increased in popularity (7). Several studies can be found in the literature that attest to their use as indicators of overt or subclinical inflammation in many diseases, and they are even considered to aid in the prognosis of cancer (8,9). Evidence also exists of the relationship between these markers and LDH (10,11). That said, the effects of these hematological parameters on TFESI outcomes in the treatment of lumbar radiculopathy have not, to our knowledge, yet been studied. Since inflammation plays an important role in LDH-induced radiculopathy; and parameters such as NLR, PLR, and SII are also associated with inflammatory processes, the aim of this study is therefore to investigate the effect of these parameters on TFESI outcomes for the management of LDH-induced radiculopathy.

MATERIAL and METHODS

The medical records of patients with unilateral lumbar radiculopathy who underwent TFESI between October 2022 and December 2022, with standard doses of corticosteroids and local anesthetics, were retrospectively reviewed with approval from the Local Institutional Review Board (reference number: E1-23-3391). The patients were diagnosed as having lumbar radiculopathy based on clinical evidence aided by lumbar MRI. Of the 150 patients who underwent TFESI, 101 patients who met the following inclusion criteria were enrolled in the study: 1) 18 years of age and over; 2) unilateral lumbar radicular pain for ≥3 months; 3) spinal nerve root compression due to LDH demonstrated by MRI at L2-3, L3-4, L4-5, or L5-S1 levels; and 4) patients unresponsive to conservative treatments. Exclusion criteria were as follows: 1) having spondylolisthesis, spondylosis, or advanced spinal stenosis on lumbar MRI; 2) a history of lumbar surgery; 3) local or systemic infections; 4) chronic inflammatory diseases, Cushing's syndrome, hypo- or hyperthyroidism, and hematological diseases; 5) having undergone steroid therapy (for whatever reason); and 6) missing follow-up visits or data.

Data including age, gender, level of injection, and results of whole blood tests performed before TFESI were obtained from hospital records. The following were all recorded from hemogram test: neutrophil (K μL^{-1}), lymphocyte (K μL^{-1}), platelet (10^3 μL^{-1}), mean platelet volume (MPV (fL)), red cell distribution width (RDW (%)), and monocytes (K μL^{-1}) data. Platelet-lymphocyte ratio, NLR and SII values were determined by the formula. Neutrophil-lymphocyte ratio was calculated by dividing the neutrophil count by the lymphocyte count. The PLR value was calculated by dividing the platelet count by the lymphocyte count, and the SII value was calculated by using the (neutrophil X platelet)/ lymphocyte formula. Pain scores were obtained before and one month after TFESI using the Visual Analogue Scale (VAS) (0 = "no pain" and 10 = "worst imaginable pain"). Therapeutic success was defined as a ≥50% decrease in VAS scores at one month, and the patients were divided into two groups, successful or unsuccessful, according to this criteria. Hemogram values and NLR, PLR and SII values were compared between the two groups.

TFESI Procedure

The injections were performed in an operating room under aseptic conditions and the guidance of C-arm fluoroscopy. Each patient was monitored, and vital signs were observed throughout the entire procedure (blood pressure, heart rate, SpO_2). During the procedure, the patient was placed in prone position and the abdomen was supported by a pillow. The C-arm fluoroscopy was rotated obliquely 15°-30° toward the ipsilateral, and cephalad/caudal tilt was provided so that the vertebral endplates could be observed in a straight line. After local infiltration with 0.5 mL of 1% lidocaine, a 22-G spinal needle was inserted and advanced toward the intervertebral foramen using the "safe triangle" method. The needle position was confirmed by antero-posterior and lateral views. After confirming ventral epidural contrast spread without intravascular, subarachnoid, or extra-epidural uptake with 1-2 mL iohexol in lateral and AP fluoroscopic views, 2 mL of 8 mg dexamethasone and 1 mL 2% of lidocaine were injected. All injections were performed by the same pain management specialist (Figure 1).

Statistical Analysis

Data was analyzed with Statistical Package for the Social Sciences (SPSS) 25.0 (IBM Co®. USA) and the Kolmogorov-Smirnov test was used to determine whether variables were normally distributed. Categorical data was expressed as numbers and percentages (%). Numerical variables with normal distribution are shown with mean ± standard deviation, and non-parametric distributed numerical variables are shown in the median and interquartile range (IQR: 25-75th percentile). The Chi-square test was used to compare categorical variables between two groups, and the independent samples t-test and Mann-Whitney U test were used to compare the numerical variables with or without parametric distribution between the groups. P<0.05 was accepted for statistical significance.

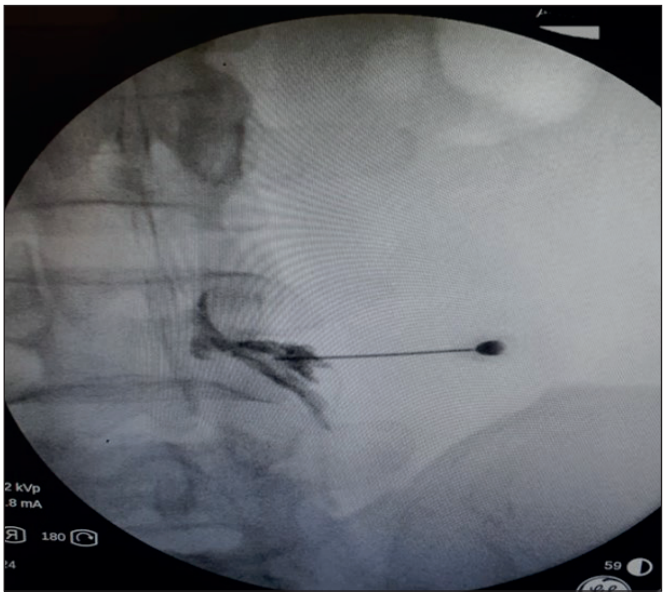

Figure 1. Contrast spread into the epidural space of fluoroscopic-guided transforaminal epidural injection.

RESULTS

The mean age of the patients is 49.43 ± 13.29, with a slight predominance of the male gender. The median pain duration is 3 months. The median value of the VAS baseline and the VAS-1st month is 8 and 3, respectively. Table I shows the demographic and clinical features of the patients. The laboratory parameters of the patients are presented in Table II.

The patients were grouped according to instances of significant pain relief, which was determined as > 50% pain reduction, and demographic and clinical variables were compared between these groups. Age was similar between

Table I. The Demographic and Clinical Features of the Patients in the Study

		n (%)	Mean ± SD or Median (IQR:25-75th percentile)
Age			49.43 ± 13.29
Sex	Female	46 (45.5)	
	Male	55 (54.5)	
Symptomatic side	Right	50 (49.5)	
	Left	51 (50.5)	
Number of injection level	One-level	38 (37.6)	
	Two-level	63 (62.4)	
Injection level	L2-3	-	
	L3-4	5 (5.0)	
	L4-5	21 (20.8)	
	L5-S1	10 (9.9)	
	S1	2 (2.0)	
	L2-3, L3-4	1 (1.0)	
	L3-4, L4-5	5 (5.0)	
	L4-5, L5-S1	39 (38.6)	
	L5-S1, S1	18 (17.8)	
Duration of pain			3.0 (3.0-8.0)
VAS-baseline			8.0 (7.0-8.0)
VAS-1st month			3.0 (1.0-6.0)

SD: Standard deviation, **IQR:** Interquartile range, **VAS:** Visual analog scale.

Table II: The Laboratory Results of the Patients In the Study

	Mean ± SD or Median (IQR:25-75th percentile)
Sedimentation	6.0 (4.0-12.5)
CRP	0.30 (0.03-0.84)
PLT	254.425 ± 64.119
Neutrophil count	5215.70 ± 1821.4
Lymphocyte	2254.0 (1820.0-2761.0)
Monocyte	490.0 (360.0-604.7)
MPV	9.1 (8.1-10.8)
RDW	13.2 (12.6-14.0)
NLR	2.12 (0.59-2.85)
PLR	107.79 (86.17-134.15)
SII	525.01 (387.89-686.64)

SD: Standard deviation, **IQR:** Interquartile range, **CRP:** C-reactive protein, **PLT:** Platelets, **MPV:** Mean plasma volume, **RDW:** Red blood cell distribution width, **NLR:** Neutrophil/lymphocyte ratio, **PLR:** Platelet/lymphocyte ratio, **SII:** Systemic inflammatory index.

groups (p=0.754); with the female ratio being higher in the unsuccessful group (p<0.01). The number of injection levels, duration of pain, and VAS baseline are all similar between groups (p>0.05). VAS-1st monthly scores were higher in the unsuccessful group, as expected. (p<0.001). Neutrophil-lymphocyte ratio is higher in the successful group. No significant differences were found between the groups regarding other laboratory parameters, including PLR and SII (Table III).

DISCUSSION

It has been suggested that mechanical compression of the herniated disc on the nerve root causes pain in radiculopathy, but this has not been fully explained. It is inappropriate to claim that mechanical compression is the sole cause of pain because in some patients the complaints and clinical findings are incompatible with MRI (12). The theory of inflammation in which it is thought that pain occurs secondary to the inflammation and irritation caused by the compression on the nerve root has therefore been suggested. There are many

Table III: Comparison of the Demographic and Clinical Data of the Groups Assigned According to Significant Pain Relief

		Successful group (n=54)	Unsuccessful group (n=47)	p
		Mean ± SD or Median (IQR:25-75th percentile) or n / %		
Age		49.81 ± 14.38	48.98 ± 12.04	0.754
Sex	Female	17 (31.5)	29 (61.7)	**<0.01**
	Male	37 (68.5)	18 (38.3)	
Symptomatic side	Right	22 (40.7)	28 (59.6)	0.059
	Left	32 (59.3)	19 (40.4)	
Number of injection level	One-level	17 (31.5)	21 (44.7)	0.172
	Two-level	37 (68.5)	26 (55.3)	
Duration of pain		3.0 (3.0-9.3)	4.0 (3.0-7.0)	0.647
VAS-baseline		8.0 (7.0-8.0)	8.0 (7.0-8.0)	0.452
VAS-1st month		1.0 (0.0-2.0)	6.0 (5.0-7.0)	**<0.001**
Sedimentation		6. 0 (3.0-11.3)	8.0 (5.0-16.0)	0.116
CRP		0.32 (0.05-0.88)	0.21 (0.0-0.70)	0.264
PLT		252.159 ± 64.51	257.029 ± 64.25	0.705
Neutrophil		5365. 0 (3947.5-6622.5)	4810.0 (3413.0-5846.0)	0.083
Lymphocyte		222.5 (182.5-272.8)	226.0 (181.0-284.0)	0.886
Monocyte		490.0 (359.4-630.5)	500.0 (360.0-574.5)	0.954
MPV		9.2 (8.1-10.9)	9.1 (8.2-10.4)	0.951
RDW		13.1 (12.5-13.9)	13.3 (12.6-14.3)	0.309
NLR		2.34 (1.70-3.17)	1.79 (1.51-2.57)	**0.026**
PLR		106.30 (83.40-141.97)	107.79 (87.65-133.16)	0.935
SII		585.08 (407.30-765.86)	509.99 (351.24-655.97)	0.119

SD: Standard deviation, **IQR:** Interquartile range, **CRP:** C-reactive protein, **PLT:** Platelets, **MPV:** Mean plasma volume, **RDW:** Red blood cell distribution width, **NLR:** Neutrophil/lymphocyte ratio, **PLR:** Platelet/lymphocyte ratio, **SII:** Systemic inflammatory index.

publications that show the presence of inflammation in LDH. Marshall et al. have described auto-antibodies against the nucleus pulposus which herniate into the epidural space (13). In a systematic review, it was reported that there was a correlation between VAS scores and TNF alpha, TNFR1, IL6, IL8, and interferon-gamma levels (14). A similar study supports the idea that IL6, IL8, IL15, and type 1 interferon, all initiate pathological processes in discopathies (15).

Since the physiological response of circulating leukocytes to stress causes an increase in the number of neutrophils, as well as a decrease in the number of lymphocytes, the ratio of these two parameters to each other is used as an indicator of inflammation (16). It is therefore suggested that NLR, PLR and SII are simple markers of the inflammatory response.

There are several studies in the literature investigating the relationship between lumbar discopathy and various hematological parameters. Dagistan et al. compared the hematological parameters of 84 patients with LDH and 59 healthy adults (11). They found that NLR was similar between the groups, but RDW and MPV were statistically significantly higher in the LDH group. Satis et al. reported that hemogram parameters (lymphocyte, neutrophil, monocytes, platelets, RDW, and MPV), sedimentation, CRP, NLR and PLR are similar between patients with upper-level LDH, patients with lower-level LDH, and patients without LDH (17). Polat and Tuncer compared 50 patients with single-level LDH, 50 patients with multi-level lumbar spinal stenosis, and 50 healthy individuals for the presence of systemic inflammation (10). Their study found that NLR and PLR were significantly higher in the patient groups, as compared to the control group, and that NLR was higher in patients with multilevel lumbar spinal stenosis than those with single level LDH. They also reported that the NLR could be an indicator in understanding whether the compressed nerve tissue increased or not. Bozkurt et al. reported that preoperative and postoperative VAS scores were higher in patients with a high NLR (18). They associated increased VAS scores with the inflammatory effect of NLR, which accurately explained postoperative patient satisfaction and preoperative excruciating pain.

No other study has been located in the literature which investigates the effect of hematological parameters on TFESI outcomes in the treatment of lumbar radiculopathy. In our study, only NLR from hematological parameters was found to be significantly different in patients who benefited from TFESI, as compared to those who did not benefit from TFESI. We attributed this to the fact that patients with high NLR, an inflammation marker, responded better to steroid treatment. Our data suggest that patients with a higher NLR (severe inflammatory response) at presentation may benefit more from TFESI.

It has been reported that there is no difference between blunt and sharp needles in terms of dural puncture, headache and local pain in TFESI (19). However, the use of blunt needles in TFESI reduces vascular penetration (20). We preferred spinal needle in TFESI because it is more practical and faster. We did not experienced any complication such as vascular penetration and dural puncture.

The study has several limitations, such as its retrospective nature, short follow-up times, the absence of functional parameters such as the Oswestry disability index, and our inability to provide a cut-off value for NLR. However, this work has value as apparently the first study in the literature which investigates the effect of hematological parameters on TFESI in patients with LDH-induced radiculopathy.

CONCLUSION

Higher NLR could serve as a strong indicator for patients with LDH-induced radiculopathy who can benefit from TFESI. Our research provides an important clue in identifying patients who would benefit from TFESI treatment through the use of NLR as a fast and practical marker that can be easily obtained with a detailed complete blood count.

AUTHOR CONTRIBUTIONS

Conception or design of the work: KSS
Data collection: KSS
Data analysis and interpretation: KSS
Drafting the article: KSS
Critical revision of the article: KSS
The author (KSS) reviewed the results and approved the final version of the manuscript.

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