Is There a Link between Lumbar Disc Herniation and Hemogram Parameters?

Lomber Disk Hernisi ve Hemogram Parametreleri Arasında Bir Bağlantı Var mı?

Erkan Kilinc[1], Yasar Dagistan[2], Emine Dagistan[3], Zeliha Cosgun[3]

[1] Abant Izzet Baysal University, Faculty of Medicine, Department of Physiology, Bolu, Turkey,

[2] Abant Izzet Baysal University Hospital, Department of Neurosurgery, Bolu, Turkey

[3] Abant Izzet Baysal University Hospital, Department of Radiology, Bolu, Turkey

Abstract

Aim: Inflammatory mechanisms play a key role in the pathogenesis of back pain related to disc hernia. Mean platelet volume (MPV) and red cell distribution width (RDW) are novel and promising inflammatory markers in routine hemogram tests. In this study, we aimed to compare the MPV and RDW values of patients with lumbar disc herniation (LDH) to those of healthy subjects and symptomatic patients suffering from sciatica without radiological evidence of lumbar disc herniation.

Materials and Methods: This retrospective cohort study was carried out in the Neurosurgery Department of the Abant Izzet Baysal University Education and Research Hospital. Three groups as the controls (n=57) and LDH (n=73) and sciatica (n=20) groups were designed. Hemogram parameters including white blood cell count (WBC), hemoglobin (Hb), hematocrit (Htc), mean corpuscular volume (MCV), RDW, platelet count (PLT) and MPV were evaluated for each group.

Results: The mean MPVs of the LDH, sciatica, and control groups were 9.3±1.8 fL, 8.2±1.1 fL, and 8.4±1.0 fL, respectively. The mean MPV was significantly higher for the LDH group, compared to the sciatica and control groups (p=0.001). The mean RDWs of the LDH, sciatica, and control groups were 14.8±1.8, 13.8±1.0, and 13.7±1.2, respectively. The mean RDW was also significantly higher for the LDH group in comparison to the sciatica and control groups (p=0.001).

Discussion and Conclusion: We think that elevated MPV and RDW values might be strong indicators of LDH in patients with sciatica and that such patients should be prioritized for imaging studies. However, further prospective studies are needed to support our results.

Keywords: mean platelet volume; red cell distribution width; inflammation; lumbar disc hernia

Öz

Amaç: Enflamatuvar mekanizmalar disk hernisi ile ilişkili bel ağrısının patogenezinde önemli bir rol oynamaktadır. Rutin hemogram testlerindeki yeni ve umut vadeden enflamatuvar belirteçler ortalama trombosit hacmi (mean platelet volume—MPV) ve kırmızı küre dağılım genişliğidir (red cell distribution width—RDW). Bu çalışmada lomber disk hernisinden (LDH) muzdarip hastaların MPV ve RDW değerlerinin, sağlıklı gönüllülere ve radyolojik lomber disk hernisi bulgusu olmayan siyataljili semptomatik hastalara ait değerlerle karşılaştırılması amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif kohort çalışması Abant İzzet Baysal Üniversitesi Eğitim ve Araştırma Hastanesi Nöroşirürji Anabilim Dalı'nda gerçekleştirildi. Kontrol (n=57), LDH (n=73) ve siyatalji (n=20) grupları olmak üzere toplam üç grup oluşturuldu. Grupların beyaz küre, hemoglobin, hematokrit, ortalama korpüsküler hacim, platelet sayısı ile RDW ve MPV parametreleri değerlendirildi.

Bulgular: LDH, siyatalji ve kontrol gruplarının ortalama MPV değerleri sırasıyla 9,3±1,8 fL, 8,2±1,1 fL ve 8,4±1,0 fL olarak bulundu. LDH grubunun ortalama MPV değeri siyatalji ve kontrol gruplarınınkinden anlamlı derecede daha yüksekti (p=0,001). LDH, siyatalji ve kontrol gruplarının ortalama RDW değerleri sırasıyla 14,8±1,8, 13,8±1,0 ve 13,7±1,2 olarak bulundu. LDH grubunun ortalama RDW değeri de siyatalji ve kontrol gruplarınınkinden anlamlı derecede daha yüksekti (p=0,001).

Tartışma ve Sonuç: Yükselmiş MPV ve RDW değerleri siyataljili hastalarda LDH'ye işaret eden güçlü indikatörler olabilir ve bu yükselmiş değerlere sahip hastalar görüntüleme çalışmalarında öncelenmelidirler. Bununla birlikte bulgularımızı destekleyen daha fazla prospektif çalışmaya ihtiyaç vardır.

Anahtar Sözcükler: ortalama trombosit hacmi; kırmızı küre dağılım genişliği; enflamasyon; lomber disk hernisi

Geliş Tarihi /*Received* : 24.11.2017
Kabul Tarihi /*Accepted*: 21.12.2017

DOI: 10.21673/anadoluklin.357593

Sorumlu Yazar/*Corresponding Author*
Erkan Kilinc
Abant Izzet Baysal University, Faculty of Medicine, Department of Physiology, 14280 Golkoy, Bolu/Turkey
E mail: e_kilinc_27@hotmail.com

INTRODUCTION

Low back pain is one of the most common health problems, including the nerves, bones and muscles of the back. The point prevalence ranges from 12 to 33% in the adult general population (1), and most people experience low back pain at least once in their life. It is a complaint reported frequently in outpatient clinics of health institutions. The lifetime prevalence and annual incidence of back pain that leads to a significant individual and financial burden are estimated to be around 80% and 2%, respectively (2,3). There are many causes and factors associated with its development, including lumbar disc herniation, spinal stenosis, degenerative spondylolisthesis with stenosis, intervertebral disc degeneration without disc herniation, and post lumbar surgery syndrome (4).

Of these, lumbar disc herniation (LDH) is a mechanical disorder involving the degeneration of the intervertebral discs. It is responsible for about 3% of all painful low back syndromes (5). Herniated discs increase the pressure on the nerve root, causing weakness, numbness and pain in legs, and thus low back pain and sciatica (5). Inflammatory mechanisms are involved in the pathogenesis of back pain related to disc hernia. The literature suggests that inflammatory markers are increased in people with lumbar disc herniation (6–8). It has been suggested that inflammatory mediators may be related in the genesis of radiculopathy (9,10). The inflammatory mediators found in lumbar disc herniation include interleukin-1, interleukin-6, phospholipase A2, tumor necrosis factor-α, granulocyte-macrophage colony stimulating factor (6,8,11). In addition, most patients with LDH recover with conservative management including use of nonsteroidal anti-inflammatory drugs (12), showing that inflammation plays a key role in LDH.

Mean platelet volume (MPV) and red cell distribution width (RDW) are novel and promising inflammatory markers in routine hemogram tests. The MPV refers to the size of thrombocytes produced by the bone marrow. The RDW is the size distribution value of erythrocytes. An elevation in MPV and RDW values has been shown in inflammatory diseases (13,14). Therefore, we hypothesized that there might be a link between LDH and the inflammatory markers in routine hemogram tests.

In this study, we aimed to compare the MPV and RDW values of LDH patients to those of healthy subjects and symptomatic patients suffering from sciatica without radiological evidence of lumbar disc herniation.

MATERIALS AND METHODS

The study was designed as a retrospective cohort study and conducted in the Neurosurgery Department of our hospital with the ethical approval (decision no. 2017/51) of the Abant Izzet Baysal University's local ethics committee. One hundred and fifty individuals were enrolled. The study design included three groups: The first was the LDH group (n=73) that consisted of patients with LDH who were diagnosed on the basis of magnetic resonance imaging (MRI). The second was the sciatica (n=20) group consisting of subjects who complained of sciatica but had normal MRI findings. The third was the control group (n=57) consisting of those selected out of the healthy volunteers visiting our institution's outpatient clinics for routine check-up. The median ages of the LDH, sciatica, and control groups were 46 (21–69), 43 (25–64), and 44 (32–68) years, respectively. There were 40 men and 33 women in the LDH group, 5 men and 15 women in the sciatica group, and 28 men and 29 women in the control group. The history and laboratory data of the study population were obtained retrospectively from the computerized database of our hospital. The subjects' values of hemogram parameters including white blood cell count (WBC), hemoglobin (Hb), hematocrit (Htc), mean corpuscular volume (MCV), RDW, platelet count (PLT), and MPV were recorded. Their history of radiological findings was also obtained from the database. Patients with active infection or chronic diseases such as diabetes mellitus and hypertension and patients on medication with drugs that may affect thrombocyte indices were excluded.

Statistical analysis

The data obtained from the records were expressed in mean±SEM for homogenous variables and median (min–max) for non-homogenous variables. The statistical analysis was performed by using SPSS for Windows (version 17.0, SPSS Inc., Chicago, IL, USA).

Table 1. General characteristics and laboratory data of all groups

	General characteristics	Groups			
		LDH (n=73)	Sciatica (n=20)	Control (n=57)	p
Gender	Man (n)	40	5	28	
	Woman (n)	33	15	29	
Age (years)	Median (Min–Max)	46 (21–69)	43 (25–64)	44 (32–68)	0.53†
WBC (u/mm³)	Median (Min–Max)	6.7 (3.3–13.9)	7.5 (4.3–11.7)	7 (4.6–10.3)	0.69†
Htc (%)	Median (Min–Max)	43 (35–51)	41.1 (33.7–50)	43 (36.5–53)	0.42†
Hb (g/dl)	Mean±SD	14.6±1.4	13.9±1.7	14.4±1.3	0.12‡
MCV (fL)	Mean±SD	88±4	86±5	87±5	0.12‡
Plt (u/mm³)	Mean±SD	268±71	236±68	257±55	0.60‡
RDW (%)	Mean±SD	14.8±1.8	13.8±1.0	13.7±1.2	0.001‡
MPV (fL)	Mean±SD	9.3±1.8	8.2±1.1	8.4±1.0	0.001‡

† Kruskal–Wallis, ‡ One-way ANOVA

WBC: white blood cell; Htc: hematocrit; Hb: hemoglobin; MCV: mean corpuscular volume; Plt: platelet; RDW: red cell distribution width; MPV: mean platelet volume; SD: standard deviation; LDH: lumbar disc herniation

One-way analysis of variance (ANOVA) and Kruskal–Wallis test were used to compare the variables between the groups. $p<0.05$ was considered statistically significant.

RESULTS

There was no difference in terms of age between the groups (p=0.53). The study population showed no significant difference in terms of WBC (p=0.69), Hb (p=0.12), Htc (p=0.42), MCV (p=0.12), and PLT (p=0.60) values. The mean MPVs of the LDH, sciatica, and control groups were 9.3±1.8 fL, 8.2±1.1 fL, and 8.4±1.0 fL, respectively. While the mean MPV was significantly higher for the LDH group compared to the sciatica and control groups (p=0.001, Figure 1), there was no significant difference between the sciatica and control groups (p=0.51). The mean RDWs of the LDH, sciatica, and control groups were 14.8±1.8, 13.8±1.0, and 13.7±1.2, respectively. Similarly, while the mean RDW was significantly higher for the LDH group compared to the sciatica and control groups (p=0.001, Figure 2), there was no significant difference between the sciatica and control groups (p=0.21). The general characteristics and laboratory data of the three groups are shown in Table 1.

DISCUSSION AND CONCLUSION

We found that the RDW and MPV values were increased in the patients with LDH compared to the controls and patients with normal MRI findings of sciatica. Inflammation in herniated discs has been shown by many previous studies. It was reported that application of autologous nucleus pulposus on the sacrococcygeal cauda equina led to increased levels of substance P in the dorsal root ganglia and spinal root in pigs (9). Some experimental studies revealed that application of isolated mechanical pressure on the root did not induce pain (15), and therefore it was suggested that nucleus pulposus led to the leakage of some mediators, which in turn contributed more peripheral sensitization of nociceptors (15,16). Application of cyclic mechanical stress on the cultured nucleus pulposus and annulus fibrosus cells obtained from rats increased PGE2 synthesis in the culture supernatants (17). Moreover, in a clinical study it was determined that disc phospholipase A2 levels correlated significantly with serum levels of phospholipase A2 in patients with lumbar disc herniation (18). In line with this clinical study, Franson et al (19) reported that phospholipase A2 activity of herniated discs was increased compared to that of normal discs. Phospholipase A2 is a critical inflammatory enzyme that plays an important role in liberation of arachidonic acid from

membranes. Conversely, Cooper et al. (20) showed vascular congestion, neovascularization, and luminal platelet adhesion in the histological examination of herniated disc tissues, although they could not show inflammatory cells in these tissues. On the other hand, Kawaguchi et al. (21) studied the immune phenotypes of cells in herniated discs, and they found that inflammatory cells in damaged tissue were likely differentiated from monocytes to macrophages.

We also showed previously in another study that several inflammatory markers and cytokines were increased in herniated disc tissues (22). Our findings are in line with those of the previous studies in the literature (11,23). However, our data suggested new parameters including RDW and MPV concerning the association between proinflammatory cytokines and LDH. MPV has been introduced as a link between thrombosis and inflammation in various inflammatory conditions (24). It has also been related with overt and occult inflammatory processes (25). In line with previous studies, we found elevated MPV values in the patients with LDH, which is an inflammatory and mechanical disorder.

Speculation on the underlying mechanism of MPV elevation in LDH is possible: Herniation of the intervertebral discs promotes production of inflammatory cytokines. These cytokines may interfere with megakaryopoiesis in the bone marrow and result in the production of larger thrombocytes. Another explanation could be that inflammatory cytokines may stimulate the enlargement of the platelets in the blood. It is known that platelets in inflammation site enlarge and have granules containing cytokines and proteins such as von Willebrand factor, thrombospondin, IgG, albumin, platelet derived growth factor, factor V and α2-antiplasmin (26).

It has been reported that there is an exact association between RDW and inflammatory disorders (27). Moreover, increased RDW has been proposed to be associated with overall mortality risk in the general population (28). In parallel to the previous reports, we showed elevated RDW values in another inflammatory disease, LDH. The pathogenesis of the RDW elevation in this subset of patients remains unclear. However, we think that inflammatory cytokines secreted from the damaged disc may have a coaction with erythropoiesis in the bone marrow, and thus red cells of different sizes

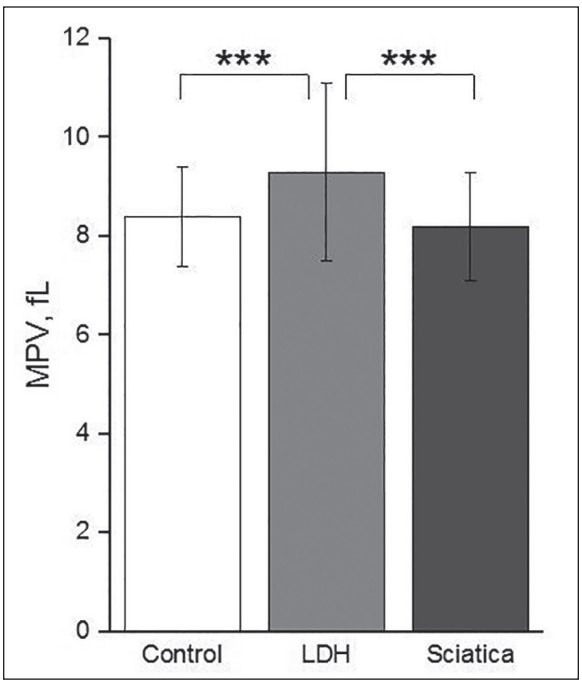

Figure 1. The mean MPVs of the LDH, sciatica, and control groups. The mean MPV was significantly higher for the LDH group compared to the sciatica and control groups.
*** p< 0.001. MPV: mean platelet volume; LDH: lumbar disc herniation.

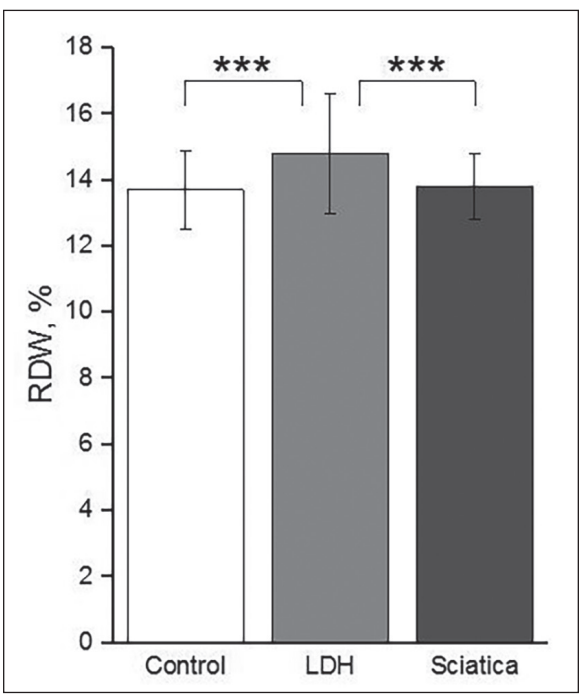

Figure 2. The mean RDWs of the LDH, sciatica, and control groups. The mean RDW was significantly higher for the LDH group compared to the sciatica and control groups.
*** p< 0.001. RDW: red cell distribution width; LDH: lumbar disc herniation.

may be produced. In our study, increased MPV and RDW levels were only observed in the subset of LDH patients. The subjects with sciatica may have failed to provide sufficient inflammatory response to affect the MPV and RDW values; we could not observe MPV and RDW changes. Interestingly, it can be concluded that patients complaining of sciatica with normal MPV and RDW values might have normal MRI results. Therefore, use of MRI should be scheduled in accordance with clinical findings and laboratory hemogram data (MPV and RDW) for cost-effectiveness, especially in new cases. In conclusion, we think that elevated MPV and RDW values might be strong indicators of LDH in patients with sciatica and that such patients should be prioritized for imaging studies.

Limitations

The two major limitations of our study were its retrospective design and the relatively small study cohort. Besides problems with patient selection, the retrospective nature of the study also makes it difficult to associate the inflammation markers with lumbar disc herniation directly. For female patients, for instance, these are similar to the mediators elevated in lumbar disc herniation during the menstrual period and may change the severity of pain. Likewise, retrospectively it is difficult to rule out the other conditions that may lead to inflammation. Another disadvantage is the non-homogeneous distribution of the study groups. As a result, further prospective studies are needed to support our results.

Conflict of Interest Statement

The authors declare no conflict of interest.

Ethical Approval Statement

This study was carried out with the ethical approval of the Abant İzzet Baysal University's local ethics committee (decision no. 2017/51).

REFERENCES

1. Walker BF. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. J Spinal Disord. 2000;13(3):205–17.
2. Demirdağ F, Ediz L, Özgür A, Tekeoğlu İ. Kronik lomber disk hernili hastaların tedavisinde tens ile elektroakupunktur tedavisinin karşılaştırılması. Van Tıp Derg. 2011;18(1):15–9.
3. Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, et al. A systematic review of the global prevalence of low back pain. Arthritis Rheum. 2012;64(6):2028–37.
4. Beyaz SG. Comparison of transforaminal and interlaminar epidural steroid injections for the treatment of chronic lumbar pain. Braz J Anesthesiol. 2017;67(1):21–7.
5. Kılıç B. Lumbar disc herniation. Adv Environ Biol. 2015;9:44–9.
6. Takahashi H, Suguro T, Okazima Y, Motegi M, Okada Y, Kakiuchi T. Inflammatory cytokines in the herniated disc of the lumbar spine. Spine (Phila Pa 1976). 1996;21(2):218–24.
7. Nygaard OP, Mellgren SI, Osterud B. The inflammatory properties of contained and noncontained lumbar disc herniation. Spine (Phila Pa 1976). 1997;22(21):2484–8.
8. Saal JS. The role of inflammation in lumbar pain. Spine (Phila Pa 1976). 1995;20(16):1821–7.
9. Goupille P, Jayson MI, Valat JP, Freemont AJ. The role of inflammation in disk herniation-associated radiculopathy. Semin Arthritis Rheum. 1998;28(1):60–71.
10. Wehling P, Bandara G, Evans CH. Synovial cytokines impair the function of the sciatic nerve in rats: a possible element in the pathophysiology of radicular syndromes. Neuro-Orthopedics. 1989;7(2):55–9.
11. Kang JD, Georgescu HI, McIntyre-Larkin L, Stefanovic-Racic M, Donaldson WF, Evans CH. Herniated lumbar intervertebral discs spontaneously produce matrix metalloproteinases, nitric oxide, interleukin-6, and prostaglandin E2. Spine (Phila Pa 1976). 1996;21(3):271–7.
12. Weinstein JN, Lurie JD, Tosteson TD, Skinner JS, Hanscom B, Tosteson AN, et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT) observational cohort. JAMA. 2006;296(20):2451–9.
13. Kisacik B, Tufan A, Kalyoncu U, Karadag O, Akdogan A, Ozturk MA, et al. Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. Joint Bone Spine. 2008;75(3):291–4.
14. Clarke K, Sagunarthy R, Kansal S. RDW as an additional marker in inflammatory bowel disease/undifferentiated colitis. Digest Dis Sci. 2008;53(9):2521–3.
15. Cavanaugh JM. Neural mechanisms of lumbar pain. Spine (Phila Pa 1976). 1995;20(16):1804–9.
16. Woolf CJ, Chong MS. Preemptive analgesia-treating postoperative pain by preventing the establishment of

central sensitization. Anesth Analg. 1993;77(2):362–79.

17. Miyamoto H, Doita M, Nishida K, Yamamoto T, Sumi M, Kurosaka M. Effects of cyclic mechanical stress on the production of inflammatory agents by nucleus pulposus and anulus fibrosus derived cells in vitro. Spine (Phila Pa 1976). 2006;31(1):4–9.
18. Piperno M, Hellio le Graverand MP, Reboul P, Mathieu P, Tron AM, Perrin G, et al. Phospholipase A2 activity in herniated lumbar discs. Clinical correlations and inhibition by piroxicam. Spine (Phila Pa 1976). 1997;22(18):2061–5.
19. Franson RC, Saal JS, Saal JA. Human disc phospholipase A2 is inflammatory. Spine (Phila Pa 1976). 1992;17(6):129–32.
20. Cooper RG, Freemont AJ, Hoyland JA, Jenkins JP, West CG, Illingworth KJ, et al. Herniated intervertebral disc-associated periradicular fibrosis and vascular abnormalities occur without inflammatory cell infiltration. Spine (Phila Pa 1976). 1995;20(5):591–8.
21. Kawaguchi S, Yamashita T, Yokogushi K, Murakami T, Ohwada O, Sato N. Immunophenotypic analysis of the inflammatory infiltrates in herniated intervertebral discs. Spine (Phila Pa 1976). 2001;26(11):1209–14.
22. Dagistan Y, Cukur S, Dagistan E, Gezici AR. Importance of IL-6, MMP-1, IGF-1, and BAX levels in lumbar herniated disks and posterior longitudinal ligament in patients with sciatic pain. World Neurosurg. 2015;84(6):1739–46.
23. Olmarker K, Larsson K. Tumor necrosis factor alpha and nucleus-pulposus-induced nerve root injury. Spine (Phila Pa 1976). 1998;23(23):2538–44.
24. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Design. 2011;17(1):47–58.
25. Gasparyan AY, Stavropoulos-Kalinoglou A, Toms TE, Douglas KM, Kitas GD. Association of mean platelet volume with hypertension in rheumatoid arthritis. Inflamm Allergy Drug Targets. 2010;9(1):45–50.
26. Harrison P, Cramer EM. Platelet alpha-granules. Blood Rev. 1993;7(1):52–62.
27. Cakal B, Akoz AG, Ustundag Y, Yalinkilic M, Ulker A, Ankarali H. Red cell distribution width for assessment of activity of inflammatory bowel disease. Dig Dis Sci. 2009;54(4):842–7.
28. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med. 2009;169(6):588–94.