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Original Article

The retrospective analysis of platelet-rich plasma and corticosteroid injection under epiduroscopic guidance for radiculopathy in operated or unoperated patients for lumbar disc herniation

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ABSTRACT

Objectives: Epiduroscopy is a treatment method that can be applied to operated or non-operated patients with lumbar disc pathology. The aim of our study was to investigate and compare the efficacy of corticosteroid and platelet-rich plasma (PRP) therapy that we have injected in epidural and foraminal spaces under the guidance of epiduroscopy in the operated or unoperated patients with radicular pain.

Patients and methods: The retrospective study was conducted with 62 patients (40 females, 22 males; mean age: 48±12.3 years; range, 20 to 75 years) between January 2014 and September 2020. Of the patients, 32 were unoperated, whereas 30 were operated. All the patients had radicular pain. All the patients were evaluated by the Visual Analog Scale (VAS) and the Oswestry Disability Index (ODI) at the start, on the 10th day, and at one and six months after the procedure by polyclinic control and by a phone call for their last follow-up.

Results: The VAS and ODI scores of patients treated with corticosteroid and PRP were decreased on the 10th day, at one and six months and the last follow-up, and this decrease was statistically significant.

Conclusion: Both PRP and corticosteroid injections were effective in pain scores during short-term and long-term follow-ups owing to the contribution of epiduroscopic intervention by allowing local administration of PRP or corticosteroids and analgesic agents as well as its mechanical adhesiolysis effect.

Keywords: Corticosteroid, epiduroscopy, platelet rich plasma, radiculopathy.

Patients with radiculopathy due to lumbar disc herniation are treated with medical, physical, and, less commonly, surgical therapy methods. It is known that some patients do not benefit from medical and physical therapy techniques despite the absence of a pathology requiring surgical therapy, and some patients suffer persistent radiculopathy even after a technically successful surgical treatment.

The clinical approach for the relief of radicular pain due to degenerative spine is diverse. The treatments are oriented to reduce the pain to a tolerable level. Even though epidural corticosteroid injections have become a standard in the pain management algorithm of conditions related to low back and radicular pain in the last 30 years, their efficacy is controversial.[1]

Platelet-rich plasma (PRP) at high concentrations supports the recovery and the anti-inflammatory process by secreting growth factors and cytokines.[2,3] Platelet-rich plasma injections have attracted attention as a new treatment method in orthopedic and rheumatologic diseases, such

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as osteoarthritis, tendinopathies, and ligament ruptures.[4] There is limited data on their efficacy in the treatment of intervertebral disc degeneration and low back pain.[5] Although, their therapeutic role in discogenic and facet joint pain is promising,[6] the efficacy of PRP injections applied to the epidural space on radiculopathy is not yet clear. Baig et al.[7] mentioned that the epidural space is an undiscovered area for PRP injections in the treatment of radiculopathy and that they found only two clinical studies on using PRP injections instead of using steroids in their literature review.[8,9] Platelet-rich plasma therapy is an effective treatment method despite debates on its efficacy and has an advantage, the absence of marked side effects.[5,7,8,10]

An opportunity is present for the diagnosis and application of the appropriate treatment by having a direct view of the complicated site since the spinal epidural area is directly in the field of vision with the use of epiduroscopic surgical technique as a minimally invasive endoscopic method.[11,12] The fiberoptic endoscope used in the process of this technique allows the implementation of therapeutic interventions in the epidural space, such as target-oriented drug treatments.[12]

In the literature, there is no study on a lumbar epidural PRP injection under epiduroscopic guidance for radiculopathy due to lumbar disc pathology. This study aimed to investigate the effectiveness of PRP in patients with radicular pain, which has not been attempted, and compare it with corticosteroids, the effectiveness of which has been proven in many studies.

PATIENTS AND METHODS

Sixty-two patients (40 females, 22 males; mean age: 48±12.3 years; range, 20 to 75 years) who underwent an epiduroscopy procedure at the Private Yalova Hospital, Bursa Yüksek Ihtisas Training and Research Hospital and Bursa City Hospital between January 2014 and September 2020 were retrospectively analyzed. The study included 32 patients with surgically unoperated disc pathology and unrelieved radiculopathy despite the application of medical and physical treatment methods for at least three months and 30 patients with unrelieved radiculopathy despite surgical treatment. The patients did not have any motor deficits. Patients with only low back pain, those without radicular pain, and patients who needed surgery were excluded from the study. Magnetic resonance imaging revealed epidural fibrosis in patients with failed lumbar surgery, whereas pathologies such as bulging or disc protrusion were encountered in the surgically unoperated patients. The demographic data of the treated patients are summarized in Table 1. Epiduroscopy procedure was administered in all the patients under local anesthesia and sedation. None of the patients were applied a corticosteroid or narcotic analgesic before or after their epiduroscopy. All the patients were evaluated by the Visual Analog Scale (VAS) and the Oswestry Disability Index (ODI) at the start, on the 10th day, and at one and six months after the procedure by polyclinic control and by a phone call for their last follow-up. All the patients were discharged on the same date.

Procedures

Platelet-rich plasma was prepared during the procedure under sterile circumstances while the patient was in the operating theatre. A 54 mL venous blood sample obtained from the patient was mixed with 6 mL of the anticoagulant acid citrate dextrose and put into a specially designed sterile disposable tube. It was centrifuged at 3200 rpm for 10 min, and approximately 7-8 mL of PRP was obtained. In the meantime, the patient was laid down on the operating table in the prone position. The sedation was achieved using midazolam. Under fluoroscopic guidance, a 0.9 mm fiber optic endoscope (Myelotec Inc., Roswell, GA, USA) was inserted into the epidural space using Seldinger's technique after local anesthesia was induced using 2 mL of prilocaine. The endoscope

TABLE 1
The demographic data of the treated patients

	Total (n=62)			PRP (n=31)			Corticosteroid (n=31)			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			48.2±12.3			49.6±13.0			46.8±11.6	0.385
Sex										0.111
Female	40	64.52		23	74.19		17	54.84		
Male	22	35.48		8	25.81		14	45.16		

PRP: Platelet-rich plasma; SD: Standard deviation.

TABLE 2
Distribution of patients according to the follow-up period and lumbar level

	Total (n=62)					PRP (n=31)					Corticosteroid (n=31)					
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*
Follow-up time (month)			35.7±23.6	23	7-81			15.1±4.6	15	7-22			56.4±15.2	49	24-81	<0.001
Lumbar Level																
L3-L4	11	17.74				6	19.35				5	16.13				
L4-L5	47	75.81				24	77.42				23	74.19				
L5-S1	34	54.84				17	54.84				17	54.84				

PRP: Platelet-rich plasma; SD: Standard deviation.

TABLE 3
Visual Analog Scale and Oswestry Disability Index scores of the patients treated with corticosteroid

	Pre-procedure			10th day			1st-month			6th-month			Last follow-up		
Corticosteroid	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max
VAS score (n=31)	8.7±1.0	9*	7-10	3.7±2.6	3	1-9	3.4±2.8	2	0-9	3.7±3.1	2	0-9	4.3±2.8	3.50	1-10
ODI score (n=31)	62.1±5.0	60*	55-72	32.5±15.6	28	14-62	30.2±16.8	24	10-62	32.8±18.3	24.50	10-66	36.8±16.3	31.50	14-66

ODI: Oswestry Disability Index; SD: Standard deviation; VAS: Visual Analog Scale; * Different from all others, p<0.001.

TABLE 4
Visual Analog Scale and Oswestry Disability Index scores of the patients treated with platelet-rich plasma

	Pre-procedure			10th day			1st-month			6th-month			Last follow-up		
PRP	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max
VAS score (n=31)	8.9±0.9*,**	9	7-10	8.4±1.4	9	3-10	4.5±2.0	5	1-9	4.2±2.3	4	0-10	3.8±2.3	3	0-9
ODI score (n=31)	63.7±5.3	64*,**	54-72	60.9±9.1	60	22-72	33.9±13.1	34	16-70	32.6±14.4	30	16-70	31.0±15.5	28	14-70

ODI: Oswestry Disability Index; PRP: Platelet-rich plasma; SD: Standard deviation; * Different 10th day, p<0.01; ** Different from 1st month, 6th month and last follow up, p<0.001.

was forwarded in the epidural space by direct visual control, and distance determination was performed by fluoroscopy. Epidural space was examined by inflation with saline infusion. The adhesions were lysed with the mechanical movement of the tip of the video-guided catheter and forcible injection of saline into the epidural space. Finally, the procedure was ended after injecting approximately 8 mL of PRP into the foraminal and epidural spaces within the complicated distance in one group, whereas 2 mL of bupivacaine and 1 mL of prilocaine diluted with serum physiological and 40 mg methylprednisolone were administered into the foraminal and epidural spaces in the other group. The same amount of PRP and steroid was applied in multilevel procedures.

Statistical analysis

The power analysis was performed using the G*Power version 3 software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany).[13] The study conducted by Bhatia and Chopra[8] was used as a reference to determine the minimum sample size needed for the priori power analysis. The effect size value was calculated as 0.62 after the analysis performed for the 1-h VAS measurements after the preoperative period and perioperative period VAS measurements. Using the relevant effect size value, the required minimum sample size was determined as 30 for each study group when the type I error level was targeted as 5% and the statistical power as 85%. The IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The Shapiro-Wilk test was used to assess whether the variables follow a normal distribution. Continuous variables were presented as mean ± standard deviation and median (minimum-maximum) values. Categorical variables were reported as numbers (%). According to the normality test results, the Wilcoxon signed-rank test was compared to the pre-and postoperative values. In comparisons performed using the Wilcoxon signed-rank test (preprocedure *vs.* 10th day, preprocedure *vs.* first month, preprocedure *vs.* sixth month, and preprocedure *vs.* the last follow up), the Bonferroni correction was applied and the adjusted type I error rate value was accepted as $\alpha^*=0.013$. The Mann-Whitney U test and independent samples t-test were used for comparisons between the study groups. A chi-square test was used to compare the sex distribution between the PRP and corticosteroid groups. A p value of <0.05 was considered statistically significant.

RESULTS

The age and sex did not differ between the study groups (p=0.385 and p=0.111, respectively). The median follow-up duration was 49 months (range, 24 to 81 months) in the patients treated with corticosteroids and 15.1 months (range, 7 to 22 months) in the patients treated with PRP. It was determined that the follow-up period was higher in the group treated with corticosteroids (p<0.001). The highest number of procedures was applied to the lumbar disc level of L4-5 (Table 2). The analysis results revealed a statistically significant reduction in the VAS and ODI scores at all measurements in the patients treated with a corticosteroid (Table 3). The VAS and ODI scores of the patients treated with PRP

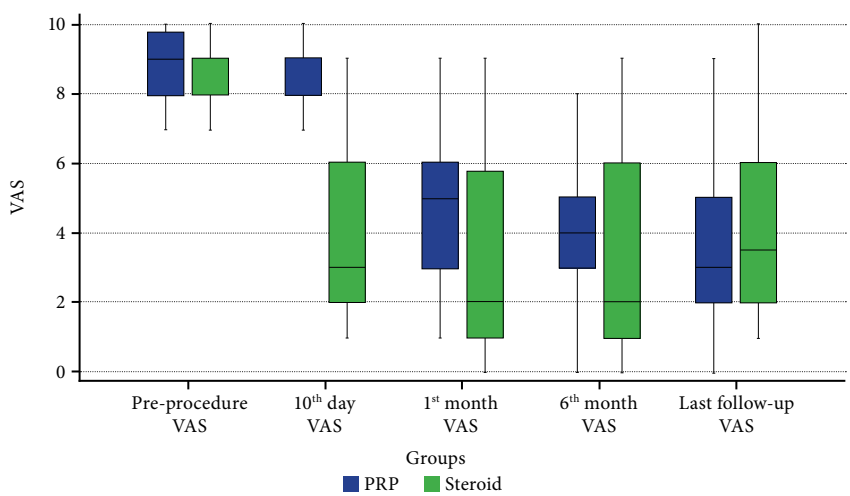

Figure 1. VAS scores of the study groups.
VAS: Visual Analog Scale; PRP: Platelet-rich plasma.

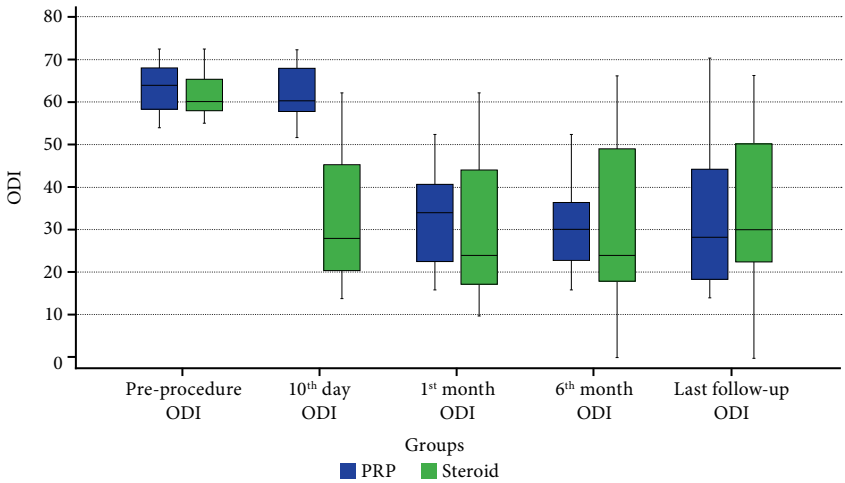

Figure 2. ODI scores of the study groups.
ODI: Oswestry Disability Index; PRP: Platelet-rich plasma.

were also found to be decreased at all measurements in a statistically significant manner (Table 4). The VAS and ODI scores started to decrease significantly from the first month in the patients treated with PRP, whereas VAS and ODI scores started to significantly decrease beginning on the 10th day after the procedure in the patients treated with corticosteroid therapy (Figures 1 and 2). Accordingly,

TABLE 5
The comparison between the operated and unoperated patients in terms of VAS and ODI in the corticosteroid group

	Operated (n=13)			Unoperated (n=18)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Corticosteroid VAS							
Pre-procedure	8.2±0.9	8	7-10	9±0.8	9	8-10	0.022
10th day	3.4±2.4	2	1-8	4±2.7	3	1-9	-
1st month	3.2±2.5	2	1-8	3.5±3.0	2	0-9	-
6th month	3.7±2.8	2.50	1-9	3.8±3.4	2	0-9	-
Last follow-up	4.8±2.0	5	2-9	3.9±3.3	2	1-10	-
10th day → pre-procedure	-4.8±2.4	-5	-8-0	-5±2.9	-6	-9-0	0.679
1st month → pre-procedure	-4.9±2.4	-5	-9-0	-5.5±3.2	-6.5	-10-0	0.373
6th month pre-procedure	-4.4±2.7	-5	-9-0	-5.2±3.5	-6.5	-10-0	0.305
Last follow up→ pre-procedure	-3.4±2.1	-3	-8-0	-5±3.3	-6	-9-1	0.094
Corticosteroid ODI							
Pre-procedure	60.2±4.5	58	55-70	63.4±5.0	62.5	56-72	0.062
10th day	29.7±13.9	24	14-58	34.6±16.8	30	14-62	-
1st month	28.9±14.3	24	14-58	31.1±18.7	22.5	10-62	-
6th month	32.4±16.4	28.50	14-60	33±19.9	24.5	10-66	-
Last follow-up	40.2±12.1	40	20-60	34.2±18.8	25	14-66	-
10th day → pre-procedure	-30.5±14.2	-33	-50-0	-28.8±18.2	-32	-56-0	0.890
1st month → pre-procedure	-31.4±15.1	-33	-56-0	-32.3±20.0	-38	-60-0	0.594
6th month pre-procedure	-30.3±19.4	-31	-64-0	-30.4±20.8	-37.5	-60-1	0.828
Last follow up→ pre-procedure	-20±13.4	-18	-45-0	-31.1±20.3	-34.5	-65-2	0.106

VAS: Visual Analog Scale; ODI: Oswestry Disability Index; SD: Standard deviation.

TABLE 6
The comparison between the operated and unoperated patients in terms of VAS and ODI in the PRP group

	Operated (n=17)			Unoperated (n=14)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
PRP VAS							
Pre-procedure	8.88±0.86	9	7-10	8.86±1.03	9	7-10	0.953
10th day	8.24±1.60	9	3-10	8.57±1.02	9	7-10	-
1st month	4.24±2.17	4	1-9	4.86±1.66	5	1-7	-
6th month	3.94±2.16	3	1-9	4.43±2.47	5	0-10	-
Last follow-up	3.88±2.52	3	1-9	3.71±2.20	4	0-8	-
10th day → pre-procedure	-0.65±1.22	0	-5-0	-0.29±0.61	0	-2-0	0.399
1st month → pre-procedure	-4.65±2.21	-5	-8-0	-4±1.71	-4	-8 – -1	0.186
6th month pre-procedure	-4.94±2.19	-6	-8-0	-4.43±2.38	-5	-9-0	0.356
Last follow up→ pre-procedure	-5±2.32	-6	-8 – -1	-5.14±2.38	-6	-9 – -2	0.891
PRP ODI							
Pre-procedure	63.76±4.83	66	56-72	63.57±5.98	64	54-72	0.922
10th day	59.71±11.25	60	22-72	62.43±5.45	63	54-70	-
1st month	33.24±15.93	30	16-70	34.64±9.23	37	16-50	-
6th month	31.71±16.22	25	16-70	33.57±12.22	33	16-60	-
Last follow-up	32.24±18.59	25	16-70	29.43±11.15	30	14-50	-
10th day → pre-procedure	-4.06±10.60	0	-44-1	-1.14±3.01	0	-10-0	0.518
1st month → pre-procedure	-30.53±14.20	-33	-48-0	-28.93±10.92	-30	-54 – -8	0.377
6th month pre-procedure	-32.06±14.25	-37	-48-0	-30±14.48	-35	-54-0	0.518
Last follow up→ pre-procedure	-31.53±16.13	-37	-50 – -2	-34.14±14	-40	-56 – -9	0.739

VAS: Visual Analog Scale; ODI: Oswestry Disability Index; PRP: Platelet-rich plasma; SD: Standard deviation.

a statistically significant improvement was observed during the follow-up durations of both groups. In addition, no statistically significant difference was found between the operated and unoperated patients in terms of VAS and ODI scores in the corticosteroid treatment group (Table 5). No statistically significant difference was present between the operated and unoperated patients in terms of VAS and ODI scores also in the PRP treatment group (Table 6). Thus, it was statistically demonstrated that all the operated and unoperated patients showed the same favorable response to corticosteroid and PRP treatments.

DISCUSSION

This retrospective study has demonstrated that similar relief and functional improvement were achieved in patients with lumbar radiculopathy treated with PRP into the epidural and foraminal spaces under epiduroscopic guidance, as obtained in the patients who were treated with a corticosteroid. No critical complication was encountered after the treatments of both corticosteroid and PRP. To our knowledge, there is no other previous study that has compared the treatments of corticosteroid and PRP in the epidural and foraminal spaces under epiduroscopic guidance for lumbar radiculopathy.

Inflammation is a term that involves clinical, physiological, and molecular events accompanied by pain. The release of proinflammatory cytokines, extracellular matrix catabolism, and cellular death are just the visible aspects of the entity.[14] Significant increases have been reported in the levels of proinflammatory cytokines such as growth-related oncogene-α, soluble intercellular adhesion molecule-1, interferon-c, tumor necrosis factor-α, interleukin (IL)-1β, IL-6, and IL-17 in the literature.[15] Contrarily, anti-inflammatory cytokines IL-4 and IL-10 have analgesic characteristics.[14]

Platelet-rich plasma is composed of a thrombocyte concentrate obtained by the removal of cellular blood components with centrifugation of autologous complete blood to increase the concentration

of thrombocytes.[16] Its components include thrombocytes, leukocytes, and red blood cells. Thrombocytes mediate the anabolic effects of PRP by liberating the growth factors deposited in alpha granules.[17] As a therapeutic agent, PRP initiates self-repair processes of the body by activating the growth factor and mesenchymal stem cells to promote recovery while it modulates inflammation and reduces pain.[18] *In vitro* studies have revealed that PRP relieves pain by downregulating vital inflammatory molecules IL-6 and IL-8.[19] Platelet-rich plasma has been used to support the recovery of the tendon, ligament, muscle, and bone owing to high concentrations of cytokines, such as activated growth factors and cytokines, including platelet-derived growth factor, transforming growth factor-α, fibroblast growth factor, insulin-like growth factor-1, connective tissue growth factor (CTGF), and epidermal growth factor (EGF), as well as bioactive proteins.[6,20,21] These growth factors are needed for increasing the fibroblast or osteoblast activity while reducing cell apoptosis in the recovery process. The circulation of the newly formed tissues and blood flow increase by the promotion of angiogenesis.[22,23]

These components of PRP function as humoral mediators to induce an anti-inflammatory effect and facilitate a natural recovery cascade by promoting cell division, migration and differentiation, protein transcription, extracellular matrix regeneration, angiogenesis, and collagen synthesis.[6,24-27] Furthermore, some studies have reported that PRP plays a positive role in the recovery of nerve injury and reduces neuropathic pain in addition to its anti-inflammatory impact.[28,29]

In the literature, the efficacy of PRP was demonstrated in a pilot study carried out in 2016 on a small study group with 10 diseases, in which epidural PRP was administered for radiculopathy with a short follow-up.[8] A series of clinical studies have described the efficacy of intradiscal PRP injections for lumbar pain due to disc degeneration related to therapeutic and inflammatory effects on type 1 Modic changes.[5,30-32] Singla et al.[33] compared PRP and corticosteroid injections regarding the application of PRP in patients with sacroiliac joint pain and obtained promising outcomes.

Although epidural corticosteroid injections are widely used, the debates are currently ongoing on their efficacy due to the lack of well-designed randomized-controlled studies.[34,35] However, positive results were obtained by epidural steroid injections in the relief of chronic low back pain due to lumbar spine, discogenic pain, and radicular pain.[35,36]

There is clinical evidence supporting PRP administration as a potential treatment option for degenerative spinal pain and radiculopathy.[5,6,16,33,37] Even though PRP administration is promising in the treatment of discogenic and facet joint pain, the role of the injections administered into the epidural space is not yet clear.[30]

There are some limitations to this study. The main limitation is that both operated and unoperated patients with lumbar disc herniation were evaluated in the same group. We did not have a sufficient number of patients to evaluate them in separate groups. However, the common feature of these patients was that they all had radicular pain. Although this study has demonstrated that PRP or corticosteroid injected into the epidural space in these patients with radicular pain contributes to healing, larger studies are needed to confirm these findings and arrive at a definitive conclusion.

In conclusion, this study has shown that the administration of PRP or corticosteroid injection into the epidural and foraminal space under epiduroscopy guidance can be considered an effective and reliable method in patients with radiculopathy who underwent failed lumbar surgery and patients with lumbar disc herniation and radiculopathy who received physical therapy.

Ethics Committee Approval: The study protocol was approved by the Bursa City Hospital Ethics Committee (date/no: 21.10.20-2020-9/3). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest: The author declared no conflicts of interest with respect to the authorship and/or publication of this article.

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