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Original Article *Özgün Araştırma*

MAY SINGLE ONE LEVEL INTRADISCAL AUTOLOGOUS PLATELET RICH PLASMA INJECTION PLAY A ROLE IN THE TREATMENT OF DISCOGENIC PAIN?
RESULTS AT SIX MONTH FOLLOW-UP

Bir Seviye Tek Sefer İntradiskal Otolog Plateletten Zengin Plazma Enjeksiyonu Diskojenik Ağrı Tedavisinde Rol Oynayabilir mi? 6. Ay Takip Sonuçları

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ABSTRACT

Objective: Low back pain is spreading both in older and younger people in a fast manner. Discogenic pain resulting from degeneration of the intervertebral disc is responsible for 40% or more of the cases of low back pain. We hypothesized that single one level intradiscal autologous platelet rich plasma (PRP) injection might provide remarkable pain relief and return to pre-illness activity level in the patients suffering from discogenic pain.

Material and Methods: Twenty-two patients underwent injections of just one 3ml dose of PRP into one intervertebral disc space (single one level intradiscal autologous PRP injection) for discogenic pain. The patients were evaluated by visual analogue score (VAS) and Oswestry Disability Index (ODI) score before intradiscal PRP treatment and at six months after intradiscal PRP treatment.

Results: The average pre-treatment VAS and ODI scores were 5.6±1.0 and 55.0% ± 11.6% respectively. The average VAS and ODI scores at six months after intradiscal PRP treatment were 1.3±1.0 and 23.2% ± 11.2% respectively and the differences were statistically significant ($p<0.01$).

Conclusion: The present study demonstrates that single one level intradiscal PRP injection may provide remarkable pain relief and may increase the return to pre-illness activity level in the patients suffering from discogenic pain. For evaluation of the efficacy of this treatment, randomized placebo-controlled trials are needed.

***Keywords**: PRP, intervertebral, disc degeneration, low back pain, Oswestry Disability Index*

ÖZ

Amaç: Bel ağrısı hem genç hem de yaşlı nüfusta gittikçe artan bir oranda görülmektedir. İntervertebral disk dejenerasyonu neticesinde gelişen diskojenik ağrı, kronik bel ağrısı şikayetlerinin yaklaşık %40'ının sebebidir. Bizim bu çalışmadaki hipotezimiz diskojenik ağrı tedavisinde bir seviye tek sefer otolog intradiskal plateletten zengin plazma (PZP) uygulamasının hastaların fiziksel aktiviteye dönüşü ve ağrı üzerinde belirgin bir iyileşme sağlayabileceğidir.

Gereç ve Yöntemler: Diskojenik ağrı tedavisi için 22 hastaya bir seviye tek sefer 3ml intradiskal otolog platelet zengin plazma (PZP) uygulaması yapıldı. Hastalar tedavi öncesi ve tedaviden 6 ay sonra vizüel analog skor (VAS) ve Oswestry disabilite index (ODI) ile değerlendirildi.

Bulgular: Tedavi öncesi ortalama VAS ve ODI skorları sırası ile 5.6±1.0 ve %55.0 ± %11.6 idi. Tedaviden 6 ay sonra ortalama VAS ve ODI skorları sırası ile 1.3±1.0 ve %23.2 ± %11.2 idi ve fark istatistiksel olarak anlamlı bulundu ($p<0.01$).

Sonuç: Çalışmamız kronik diskojenik ağrı hastalarında bir seviye tek sefer intradiskal PZP uygulamasının hastaların fiziksel aktiviteye dönüşü ve ağrı üzerinde belirgin bir iyileşme sağlayabileceğini göstermiştir. Intradiskal PZP tedavisnin etkinliğini daha derinlemesine araştırmak için randomize plasebo kontrollü çalışmalara ihtiyaç vardır.

***Anahtar Kelimeler**: PZP, intervertebral, disk dejenerasyonu, bel ağrısı, Oswestry Disability Index*

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INTRODUCTION

Low back pain is spreading both in older and younger people in a fast manner (1). Low back pain is one of the main causes of the labour loss in the middle-aged group and contributes most to the economic burden of musculoskeletal conditions in the health care system (2,3). All the anatomic structures forming the adult vertebrae may be the source of the low back pain (4). However, discogenic pain resulting from degeneration of the intervertebral disc (IVD) is responsible for 40% or more of the cases of low back pain (5). Rest, braces, non-steroidal anti-inflammatory medications as well as physical therapy programs and surgery may be used in the treatment of discogenic pain (6). Approximately 20% of patients experience recurrence of the discogenic pain despite an appropriate treatment after an initial episode and some of them will suffer from chronic low back pain (7,8).

The IVD is merely avascular. Small arterioles around the annulus fibrosis form the scanty blood supply. The IVD relies on the passive diffusion from the adjacent vertebral bodies for nutrition (9). Because of the scanty blood supply and so restricted healing ability of the IVD, researchers have increased interest on the alternative treatment methods for discogenic pain (10).

Platelet rich plasma (PRP) is a relatively novel treatment method for some degenerative musculoskeletal diseases (11). PRP is obtained utilizing autologous blood of the patient with the aid of an automated machine using the centrifugal force. PRP contains more concentrated platelet counts than in autologous blood of the patient (11). These platelets may secrete growth factors and cytokines essential for the tissue repair processes (11-13). Local high concentrations of these growth factors secreted from the higher concentration of the platelets may stimulate IVD regeneration in the case of discogenic pain where the primary pathology is the degeneration of the IVD (10,14,15).

We hypothesized that single one level intradiscal autologous PRP injection might provide remarkable pain relief and increase in return to pre-illness activity level in the patients suffering from discogenic pain. We undertook a prospective case series study to report the outcomes of single one level autologous intradiscal PRP injection for the treatment of discogenic pain.

MATERIALS AND METHODS

The study was approved by the local ethics committee (Nigde Ömer Halisdemir University Ethics Committee, date: 06.09.2019, decision number: 2019/21). The study performed prospectively however the acquired data evaluated retrospectively. Patients with low back pain admitted to the Nigde Omer Halisdemir University Teaching Hospital were evaluated by the first author between 2 January 2015 and 31 December 2017. Discogenic pain was diagnosed by using findings obtained from patient evaluations and by radiological studies that met the following criteria. Discography was not performed in any patients for the diagnosis of discogenic pain.

Clinical feature of the pain: Pain on the vertebral column, especially with restricted lomber vertebra range of motion or significant increase in the pain to centralization and peripheralization maneuvers and absence of significant referred pain caused by radiculopathy (16).

Radiological findings: Increaes intensity zone inside the IVD on T1 images, protrusion or decreased signal intensity on T2 images, or type 1 or type 2 Modic changes of an endplate on MRI and absence of severe spinal stenosis, spinal fracture, facet arthrosis or any other disease that may mimic discogenic pain (Figure 1a – 1b) (17).

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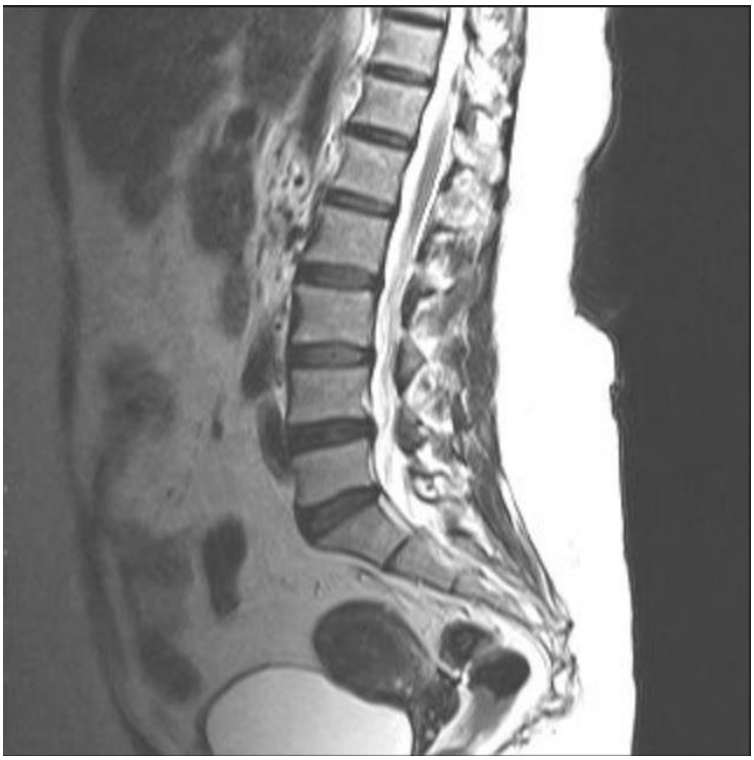

Figure 1a: Decreased signal intensity and a small disc protrusion seen on T2 MR image on L4 – L5 suggestive of discogenic pain.

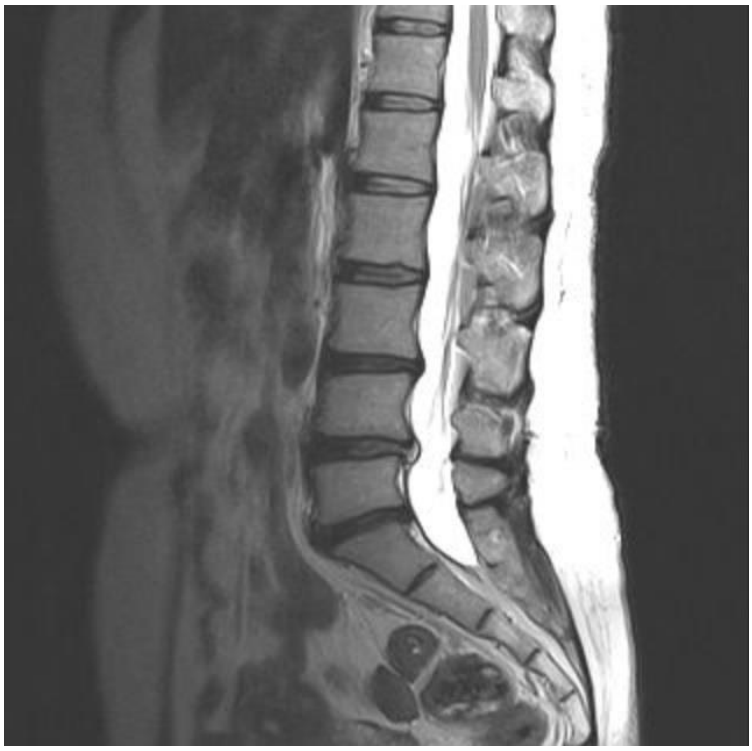

Figure 1b: Disc protrusion and high intensity zone suggestive of discogenic pain on T2 MR image of the patient on L4–L5 intervertebral disc. Decreased signal intensity implicating intradiscal water loss of L3–L4 and L5–S1 intervertebral discs are distinguished. However, no disc protrusion or type 1–2 modic changes of the endplates are seen at L3–L4 and L5–S1 intervertebral discs.

Patients suffering from discogenic pain were assessed for eligibility for the study according to inclusion and exclusion criteria (Table 1). Thirty-one patients fulfilled the criteria. Five patients refused giving consent and twenty-six patients were enrolled into the study after they gave informed consent.

Table 1: Inclusion and exclusion criteria of the study group.

Inclusion Criteria	Exclusion Criteria
• Discogenic pain persisting for >6 months • Only one level of disc degeneration or protrusion causing discogenic pain on MRI • Failure of conservative treatments for discogenic pain; rest, oral medication* and physiotherapy**	• Any kind of active infection • Pregnancy • Known bleeding disorder or current anticoagulation therapy • Any severe comorbid disease; kidney failure, hepatic failure, heart failure, uncontrolled diabetes • Non discogenic source of pain: facet arthrosis, spinal stenosis, spondylolysis or spondylolisthesis determined on MRI • Significant radiculapathy or abnormal neurologic examination • Extrusion or sequestered disk fragments on MRI • Previous spinal surgery or previous spinal fracture • Any neurological and psychiatric disorders • More than one level of disc degeneration or protrusion probably causing discogenic pain on MRI

*Diclofenac potassium (Dolorex, Abdi Ibrahim AS, Turkey) 100 mg/day, 50mg 2x1 per os for two weeks.

**Physiotherapy program was focused on patient education and strengthening exercises of the paravertebral muscles. The therapy was performed three times a week for 3 weeks in trust of a physiotherapist experienced in the field.

Diagnostic and laboratory work up including complete cell count (CBC), blood sugar, blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood sodium and potassium levels, coagulation profile were undertaken and visual analogue score (VAS) and Oswestry Disability Index (ODI) scores were obtained from all participants one week before the single one level intradiscal PRP injection.

PRP preparation was undertaken in the operating room. PRP was prepared from patients' own blood using a commercial kit (GPSIII, Biomet, UK) under aseptic conditions. Twenty-seven ml of patients own blood and 3ml anticoagulant citrate dextrose solution (ACD-A) were centrifuged for 15 minutes and 3 ml of PRP was prepared. The patients were given intravenous 1 gr/4 ml cephazoline sodium (Cezol, Deva Holding AS, Turkey) 30 minutes prior to the procedure for discitis prophylaxis and intravenous bolus 2 mg midazolam (Dormicum, Deva Holding AS, Turkey) for sedation just before beginning the PRP injection procedure under close monitorization of the patient. Under strict aseptic precautions, 5 ml local anesthetic prilocaine 2%

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(Priloc, Vem AS, Turkey) was applied under the skin and subcutaneous tissue and then a single injection of 3 ml autologous PRP was administered via interlaminar approach with 18G needle using fluoroscopic guidance in the intervertebral disc causing the discogenic pain which was determined by pretreatment MRI scans (Figure 2a–2c). After the procedure haemodynamic parameters were monitored for 20 minutes. Patients were evaluated for 1 hour after the procedure and were discharged with the advice to avoid heavy physical activities or walking long distances for 3 weeks.

Four patients were lost to follow up at six months after the intradiscal PRP treatment and 22 patients completed the study. At six months after the intradiscal PRP treatment, patients were re-evaluated and VAS and ODI scores of the patients were recorded.

Statistical Analysis

Sphericity and homogeneity of variance were controlled and then mean values of the measurements were compared by the Factorial Repeated Measures Analysis of Variance method. Assumptions for parametric tests were not available for some variables. Thus, before the analysis, transformations of these variables were performed. Compliance with the normal distribution of variables was checked with Shapiro-Wilk test. Homogeneity of groups' variances was checked by Levene's test. If parametric test assumptions were available, two independent group means were compared by Student's t test and dependent group means were compared by paired samples t test. If assumptions were not available, Mann Whitney U test was used for comparisons of independent groups' medians and Wilcoxon test was used for dependent groups. Data analyses were performed using the Statistical Package for the Social Sciences, version 19.0 (SPSS 19, Armonk, NY: IBM Corp). A p value of ≤0.05 was considered statistically significant. A p value <0.05 was considered statistically significant.

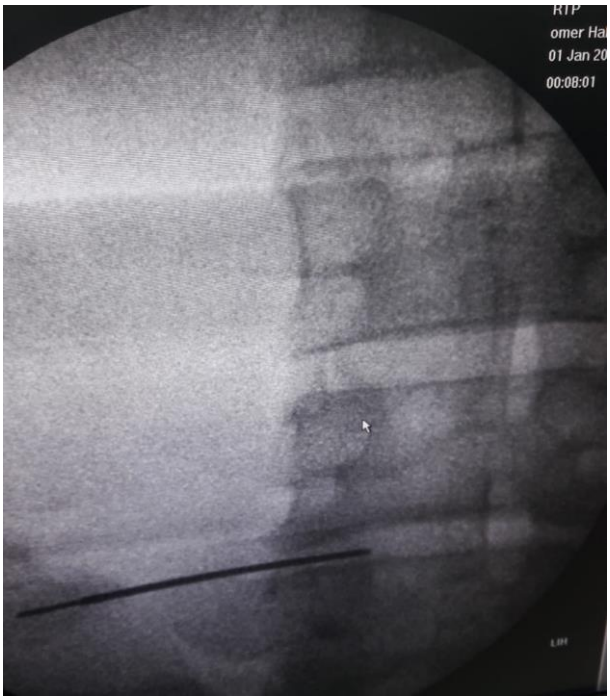

Figure 2a

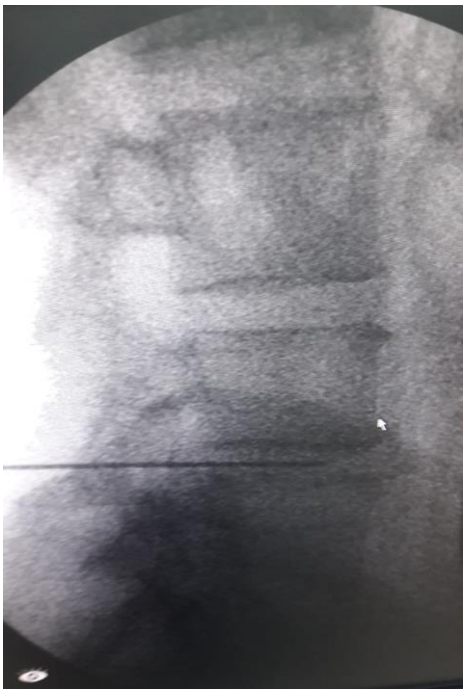

Figure 2b

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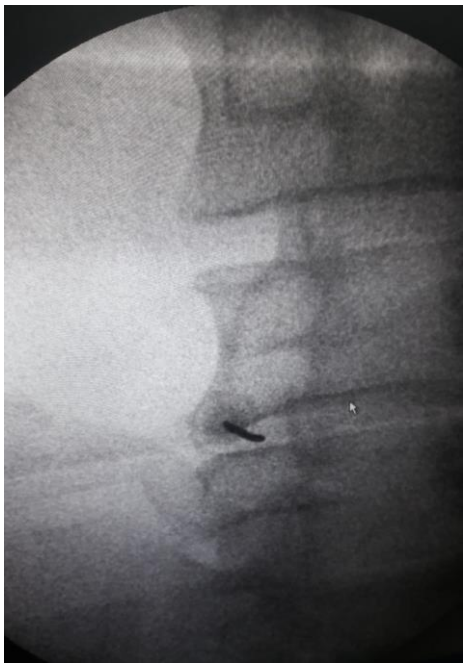

Figure 2c

Figure 2a-c: Fluoroscopic confirmation of needle position at L4–L5 intervertebral disc. a: Anteroposterior, b: Lateral and c: Oblique view of the vertebral column of the patient demonstrating the L4 – L5 intradiscal position of the needle.

RESULTS

The demographic data of the participants are listed in Table 2. The levels of discs in which PRP injections were made are listed in Table 3. There was no complication in patients treated with intradiscal PRP injection.

The average pre-treatment VAS score was 5.6±1.0 and the average VAS score at six months after intradiscal PRP treatment was 1.3±1.0 and the difference was statistically significant ($p<0.01$). The average pre-treatment ODI score was 55.0% ± 11.6%and the average ODI score at six months after intradiscal PRP treatment was 23.2% ± 11.2% and the difference was statistically significant ($p<0.01$). The pre-treatment and at six months after intradiscal PRP treatment VAS and ODI scores of all participants are shown in figures 3a – 3b respectively.

ODI scores of five patients decreased to 0–20% and ODI scores of eight patients decreased to 20–40% at six months follow up, over thirteen patients that had ODI score 40–60% before intradiscal PRP treatment. ODI scores of two patients decreased to 0–20% while scores of another two patients decreased to 20–40% in addition to another two patients whose scores decreased to 40–60% at six months follow up, over six patients that had ODI score 60–80% before intradiscal PRP treatment. ODI score of one patient decreased to 20–40% at six months follow up from 80–100% before intradiscal PRP treatment. But ODI scores of two patients did not change with intradiscal PRP treatment and stayed at 20–40% both before and at six months after intradiscal PRP treatment (Table 4).

Male patients had very slightly higher VAS scores and female patients had very slightly higher ODI scores both before treatment and at six months after intradiscal PRP treatment than the other sex in subgroups of patients according to gender, but this difference was not statistically significant ($p>0.05$). The improvement in VAS and ODI scores at six months after intradiscal PRP treatment between male and female patients also was not statistically significant ($p>0.05$) (Table 5).

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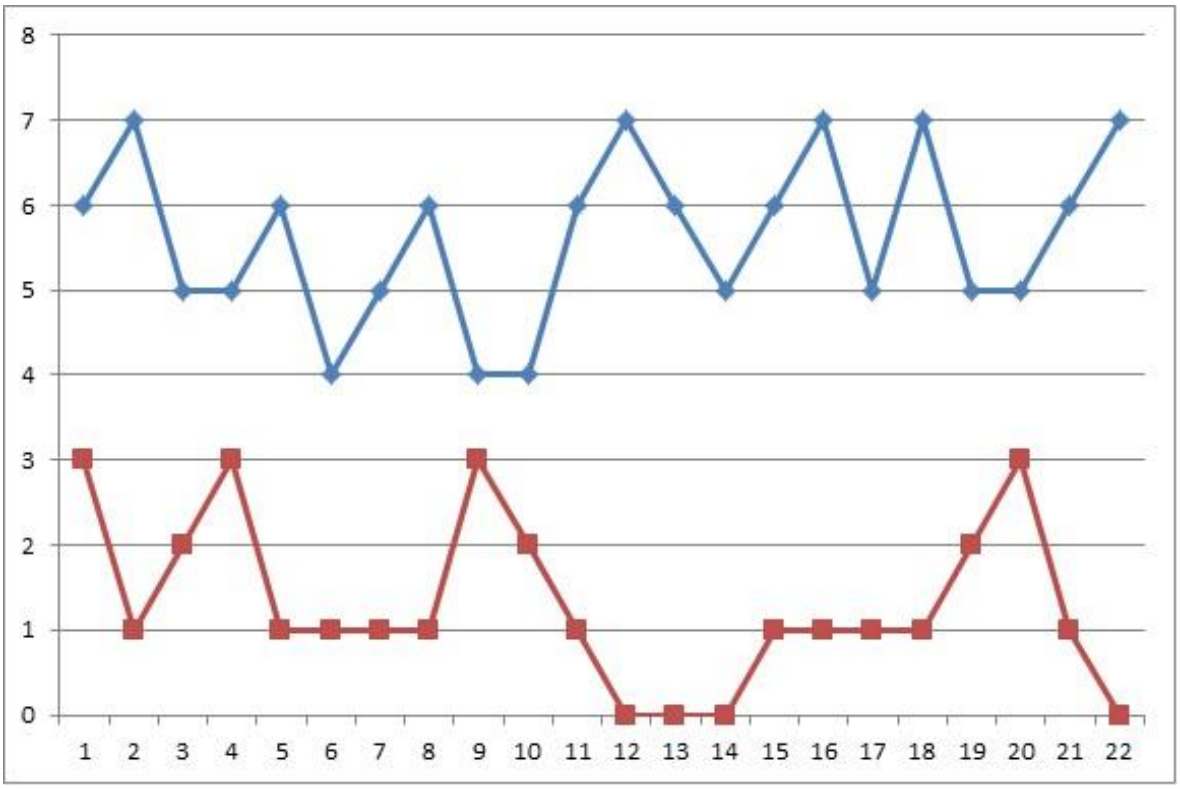

Figure 3a: The blue line represents pre-treatment and the red line represents at six months follow-up VAS scores of the participants.

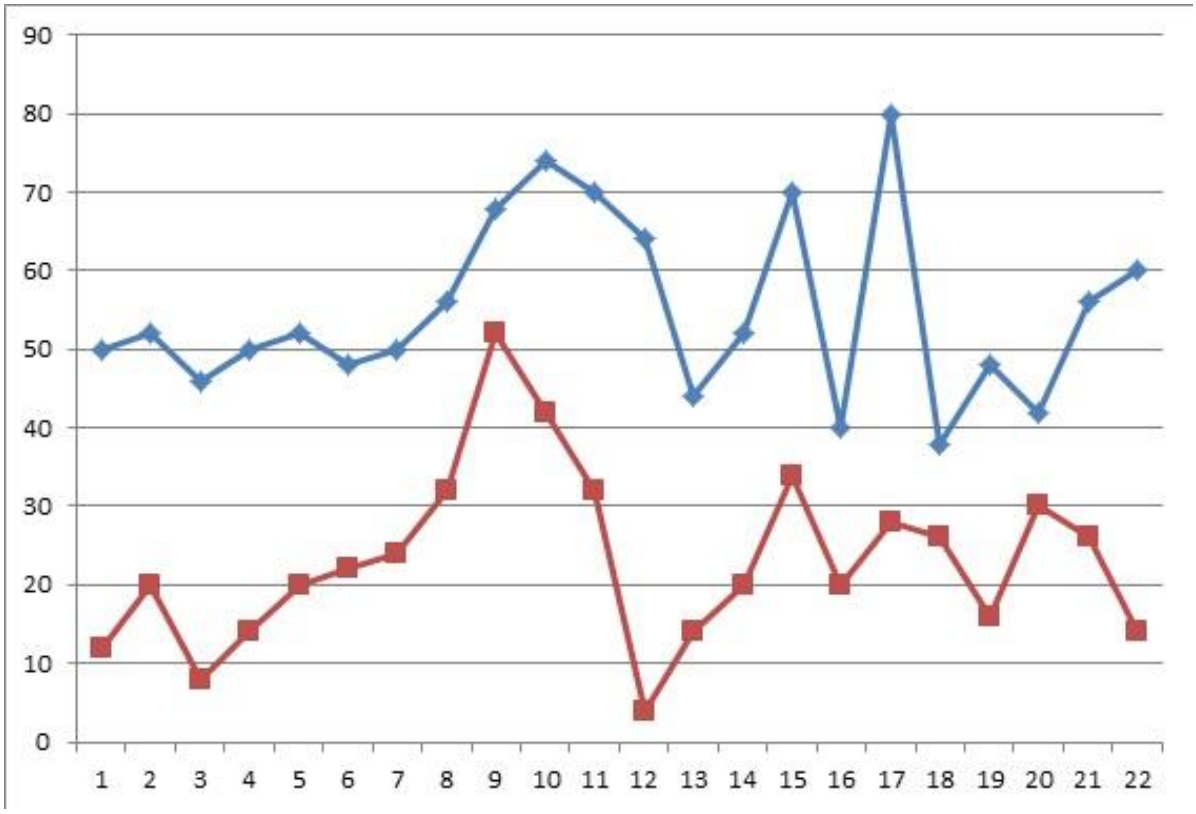

Figure 3b: The blue line represents pre-treatment and the red line represents at six months follow-up ODI scores of the participants.

Table 2: Demographic variables of the study group.

Male	9
Female	13
Age at procedure (years)	
Mean ± SD	41.7±9.7
Median	41
Minimum – Maximum	25-60
Employed	14
Unemployed	8
Insurance Status	
National Health Insurance	22
Private	0
Duration of Low Back Pain (Months)	
Median	12
Minimum – Maximum	8-14

Table 3: Intradiscal PRP injection levels.

Disc injection Levels	**Number**
T12 – L1	0
L1 – L2	0
L2 – L3	1
L3 – L4	3
L4 – L5	10
L5 – S1	8

Table 4: The distribution of participants according to ODI scores pre-treatment and at six months follow-up

Pre-treatment ODI score	6 months follow up ODI score		
	0-20%	20-40%	40-60%
0-20% (n:0)	-	-	-
20-40% (n:2)	-	2	-
40-60% (n:13)	5	8	-
60-80% (n:6)	2	2	2
80-100% (n:1)	-	1	-
Total	7	13	2
		p<0.01	

Table 5: VAS and ODI scores before treatment and at six months follow-up in the groups according to gender

		Pre-treatment VAS	6 months VAS	p value*		Pre-treatment ODI (%)	6 months ODI (%)	p value*	
Female (n=13)	Mean±SD	5.6±1.0	1.2±1.0			57.4±14.4	27.0±12.5		
	Median	6	1	<0.01		56	28	<0.01	
	Min–Max	4–7	0–3		>0.05	38–80	4–52		>0.05
Male (n=9)	Mean±SD	5.7±1.0	1.4±1.0			51.6±4.2	17.8±6.0		
	Median	6	1	<0.01		50	20	<0.01	
	Min–Max	4–7	1–3			46–60	8–26		

* The improvement in VAS and ODI scores at six months follow-up in the female and male groups were statistically significant (p<0.01). However, the improvement in VAS and ODI scores at six months after intradiscal PRP treatment between male and female patients was not statistically significant (p>0.05).

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DISCUSSION

The majority of the published literature examining the effects of the PRP treatment on the discogenic pain reported favourable results (10,18,19). The PRP treatment does not cause any major side effects because of its autologous nature and so the safety of the procedure is a significant advantage for the patients suffering from discogenic pain (10,12). In our study we did not experience any side effects or complications also.

Our results were similar with studies done by Akeda et al. and Bodor et al (18,19). Akeda et al made PRP injections in one or more level to patients suffering from discogenic pain. VAS score improvements was observed from 7.1±1.2 to 1.8±2.0 ($p<0.01$) for six months (18). In another study, Bodor et al. reported favourable effects of single intradiscal PRP injection for a period of almost one year in about 60% patients (19). In the present study we also had good results in alleviating the intensity of pain and ability to return to the pre-illness activity level.

In a 2016 study, Levi et al. published data from a study examaning the effects of autologous PRP in the treatment of discogenic pain (6). Back pain was measured using VAS and ODI scores. Although the results favour the use of PRP in discogenic pain, the results were worse than previously reported by Akeda and Bodor et al (6,18,19). According to Levi et al, the inferiority in the good and excellent results might arise from several reasons. First, Levi et al injected 0.6 ml of contrast, 0.4 ml of gentamicin, and 0.5 ml of lidocaine prior to injecting the PRP, for needle testification, infection prophylaxis, and for alleviating the pain caused from the procedure itself. However, there are some studies demonstrating a devastating effect of anesthetics and antibiotics on the cell culture medium (6). Because of this negative effect, there might be some deterioration in the results of PRP treated patients. Second, after injecting antibiotic, anesthetics and contrast matter, there was small space left for PRP injection within the IVD. Levi et al. made injections 1.5 ml of PRP for each degenerated disc in contrast to 2 ml of PRP in the study reported by Akeda et al. (6,18).

In our study, we used intravenous cephazolin, intravenous midazolam and subcutaneous prilocaine for infection prophylaxis, for sedation and for local anaesthesia before the PRP injection procedure. The needle position was testified with fluoroscopic imaging. There were three main advantages of this approach. First, in the absence of the anesthetics, antibiotics or contrast matter inside the IVD, the potential harmful effects of these drugs to nuclear cells could be avoided (6). Second, 3 ml autologous PRP was injected into the degenerated discs without difficulty as a result of more space available in the IVD. Third, the concentration of the growth factors and the platelets in the PRP were not diluted inside the IVD because of additional liquid coming from the anesthetics, antibiotics or contrast matter solutions. The superiority of improvement in VAS and ODI scores in our study in contrast to the study of Levi et al might be as a result of these factors. Indeed, more research are needed to clearly determine the standard treatment protocol.

There are several limitations in this study. First, the present study has a small number of patients. Second, discography was not performed prior to the PRP injection procedure. Because of this, there was an ineveitable error margin caused by the presuming of the patients having a discogenic pain just relying on the clinical basis and radiological imaging modalities (17). Discograpy did not performed because of the volume of contrast matter during discography would leave very small space for the PRP injection and only a small volume of PRP could be injected inside the degenerated IVD. Third, the present study had no control group. The results of the single one level

autologous intradiscal PRP injections for discogenic pain could not be compared with placebo.

The present study demonstrates that single one level autologous intradiscal PRP injection may provide remarkable pain relief and return to pre-illness activity level of the patients suffering from discogenic pain. More research is needed to clearly determine the standard treatment protocol of intradiscal PRP treatment for discogenic pain. Randomized placebo-controlled trials are needed to further evaluate the efficacy of this treatment.

Conflict of Interest: None.

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