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ORIGINAL RESEARCH

Regenerative Pain Therapy Using Platelet-Rich Plasma Compared with Steroid Injection for Spinal Disc Herniation: A Meta-Analysis

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Article Info: ABSTRACT

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Background: Radicular pain resulting from spinal conditions remains one of the most challenging problems for clinicians. This meta-analysis aimed to compare the interventional pain outcomes of platelet-rich plasma (PRP) injection versus steroid injection in patients with disc herniation.

Methods: A systematic review was conducted following PRISMA guidelines using PubMed, Science Direct, Cochrane Library, and RevMan 5.3. Three RCTs were analyzed.

Results: A total of 204 patients were included (PRP n = 101; control n = 103). There was no significant difference between the PRP and steroid for VAS (Visual Analog Scale), ODI (Oswestry Disability Index), and SF-36 scores at 3 and 6 months.

Conclusion: PRP provides similar pain reduction compared with steroid injection, with the additional advantage of potential regenerative effects. Further studies are warranted to evaluate structural regeneration

Keywords: Disc herniation; Pain; Platelet-rich plasma; Steroid.



INTRODUCTION

One of the most difficult medical issues that clinicians must treat is radicular pain that results from a spinal condition. The mechanical deformation brought on by either a herniated disc or excessive tissue proliferation, which results in both nerve root compression and nerve irritation, and the chemical mediators coming from either a ruptured disc or from nearby structures represent two essential factors that trigger inflammatory reactions and increase sensory neuron susceptibility, resulting in radicular pain. Epidural steroid injection (ESI) appears to be more successful in minimizing discomfort. enhancing functionality, and avoiding spinal surgery. 1 Nevertheless, a number of studies have revealed potentially serious negative effects, including infection, allergic reactions, and endocrine suppression. ² In the first three months, the majority of randomized studies have shown a significant improvement in pain reduction. However, conflicting results have been observed in the rate of later operations and the pain reduction of longterm follow-up. ³ Recently, platelet-rich plasma (PRP) has received recognition as an adjuvant component. Interleukin-1

receptor antagonist (IL-1Ra).

Transforming Growth Factor-1 (TGF-1), Platelet-Derived Growth Factor (PDGF), and Insulin-like Growth Factor-1 (IGF-1) are only a few of the cytokines and growth factors found in PRP. 4 PRP presents a low risk of immunogenic reactions, adverse effects, and surgical site infection because of its autologous and antimicrobial properties. ⁵ The main mechanisms were the neural regeneration pathway, the anti-inflammatory pathway, and disc resorption. PRP and platelet-rich products may have beneficial short- to long-term effects and be safe when used to treat HNP, according to several studies. ^{6,7,8}. The purpose of the current study was to study the interventional pain outcome of platelet-rich plasma injection compared with steroid injection for treating disc herniation.

METHODS

Literature search

As seen in Fig. 1, ⁹ this meta-analysis was carried out in accordance with the PRISMA recommendations. The literature search was conducted. Plateletrich plasma, steroids, disc herniation, and pain are the terms employed. Finally, from 2013 through 2023, all randomized control trials were considered.



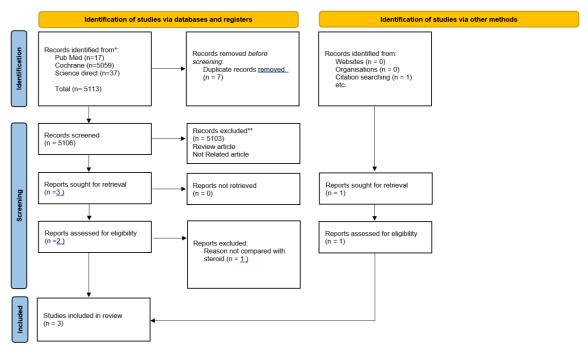


Figure 1. Record screening article with PRISMA flow chart.

Inclusion and exclusion criteria

Randomized controlled trials (RCTs) comparing PRP with steroids were included if they reported at least one of the following outcomes: VAS, ODI, SF-36 bodily pain, or SF-36 physical function. Studies with incomplete data or non-RCT designs were excluded. The studies were independently reviewed by the authors, who then extracted pertinent information and discussed each result.

Outcome and study quality

VAS Score, ODI, SF 36 bodily pain, and SF 36 physical function are among the results that were evaluated. Using a scale from 0 to 5, the Jadad score was used to evaluate the RCTs' quality. Additionally, when the score was >4, 3-4, and 3, respectively, it was deemed to be of

high, moderate, and low quality.

The score evaluation is shown in Table 1 ¹⁰. The Oxford Center for Evidence-Based Medicine's accessible criteria ¹¹ were used to evaluate the level of evidence for each study.

Statistical analysis

Each parameter was calculated using Review Manager version 5.3 statistical analysis, and data from several studies were integrated using Mantel-Hanzel methods. Dichotomous or categorical data were used, and they were reported as an OR with a 95% confidence (CI). interval Additionally, the. heterogeneity of the studies is examined using the Cochrane Chi-Square test and inconsistency^{I2}. Heterogeneity considered significant when I2 > 50%, and



a P-value of 0.05 was used to define random and fixed effect models, statistical significance. When respectively, were utilized heterogeneity was greater than 50%,

Table 1 RCT for meta analysis

			Study			Case s n	
Author	Country	Intervention	Design (Evidenc e Level)	Jadad Score	Eligible Criteria	PRP	Control
Wongjarup ong. et al 2023 [12]	Thailand	PRP vs Control	RCT (1b)	5	epidural injections were performed under a C-arm fluoroscopy. needle-end was located and checked by contrast media, either 2 mL of PRP followed by NSS 0.5 ml, or total of 2ml of 1% lidocaine with 40 mg triamcinolone	15	15
Xu et al 2021 [13]	China	PRP vs Control	RCT (1b)	5	ultrasound-guided transfor- aminal injection using an ultrasonic device. the injection was administered (steroid group: 2 ml betametha- sone+0.5 ml 0.9% sterile saline+0.5 ml 2% lidocaine; PRP group: 3 ml autologous PRP)	61	63
Lopez et al 2020 [14]	Spain	PRP vs Control	RCT (1b)	5	PRP group: patient injected with total of 20 mL LR-PRP mixture (16.5 mL of LR-PRP and 3.5 mL of non-ionic iohexol contrast medium). Steroid/control group: epidural injection of 20 mL corticosteroid mixture (60 mg of triamcinolone acetonide and 3.5 mL iohexol contrast medium in normal saline)	25	25



RESULT

Baseline characteristic

With the final screening outcomes of three studies, a total of 5113 related articles and four from additional sources were examined in the form of a bibliography. A total of 204 patients made up the sample. Additionally, as indicated in Figure 1, this comprises 101 samples from the PRP group and 103 samples from the control group.

The features of the studies that were considered are displayed in Table 1 [12,13,14]. Three RCTs had an evidence base determination level of 1b, and Jadad scores of 5 indicated that the trials had acquired a significant degree of quality.

Visual Analogue Scale (VAS)

There was no significant difference between PRP and steroid groups for VAS at 3 months (MD 0.21; 95% CI -0.61 to 0.19; p = 0.30) and 6 months (MD 0.36; 95% CI -0.59 to 1.31; p = 0.46). Similar findings were observed for ODI and SF-36 scores.

Figure 2 also shows two studies with 103 patients in the control group and 101 patients in the PRP group. The PRP group has no significant difference on VAS at 6 months (MD 0.36; 95% CI, -0.59 to 1.31; p = 0.46), and no heterogeneity is reported (I2 = 94%)

Functional Score (Oswestry Disability Index, ODI)

Functional scores (Oswestry Disability Index, ODI) were compared in two studies, as shown in Figure 3. Data showed no significant difference in ODI in the PRP group compared with the steroid goup of patients (MD -0.38; 95% CI, -4.67 to 3.91; p = 0.86), and heterogeneity (I2 = 59%) was reported.

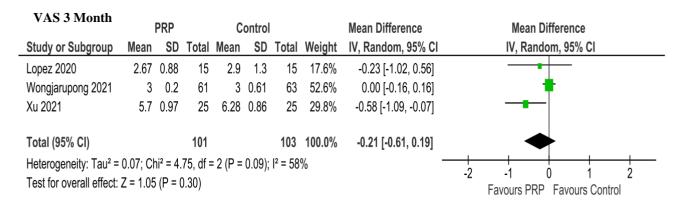
Two studies reported functional scores (Oswestry Disability Index, ODI), as shown in Figure 3. Pooled data showed no significant difference in ODI in the PRP group compared with the steroid group of patients (MD -2.93; 95% CI, -8.40 to 2.54; p = 0.29) with heterogeneity (I2 = 80%).

Functional Score (SF 36 Bodily Pain 6 month)

The functional scores from two trials utilizing the SF 36 bodily pain 6 months are shown in Figure 4. The SF 36 bodily pain score at six months was not significantly different between the PRP group and the steroid group of patients, according to the combined data (MD - 0.82; 95% CI, -3.61 to 1.97; p = 0.57; I2 = 9%).

Figure 4 Data showed no significant difference in SF 36 physical function 6 months in the PRP group compared with the steroid goup of patients (MD 11.21; 95% CI, -13.21 to 35.63; p = 0.37), and heterogeneity (I2 = 95%) was reported.





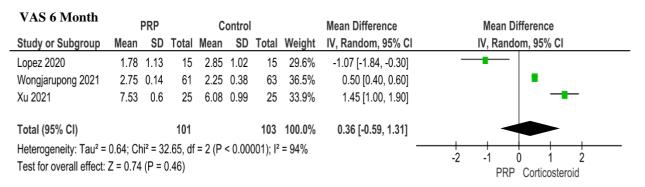


Figure 2. Forest plot of VAS 3 and 6 months

ODI 3 Month PRP		Control					Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Wongjarupong 2021	18.07	8.06	15	21.64	7.92	15	32.0%	-3.57 [-9.29, 2.15]			
Xu 2021	21.37	3.62	61	20.25	4.91	63	68.0%	1.12 [-0.40, 2.64]	•		
Total (95% CI)			76			78	100.0%	-0.38 [-4.67, 3.91]	•		
Heterogeneity: Tau ² = 6.44; Chi ² = 2.41, df = 1 (P = 0.12); I^2 = 59% Test for overall effect: Z = 0.17 (P = 0.86)								-20 -10 0 10 20 PRP Control			

ODI 6 Month	PRP		Control				Mean Difference	Mean Difference					
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl		IV, Random, 95% CI			
Wongjarupong 2021	15.07	7.79	15	21.3	5.21	15	41.7%	-6.23 [-10.97, -1.49]			-		
Xu 2021	20.75	4.33	61	21.32	3.68	63	58.3%	-0.57 [-1.99, 0.85]			•		
Total (95% CI)			76			78	100.0%	-2.93 [-8.40, 2.54]			•		
Heterogeneity: $Tau^2 = 12.83$; $Chi^2 = 5.02$, $df = 1$ (P = 0.03); $I^2 = 80\%$ Test for overall effect: $Z = 1.05$ (P = 0.29)								-50	-25	0 PRP Co	25 ntrol	50	

Figure 3. Forest plot of ODI 3 and 6 months



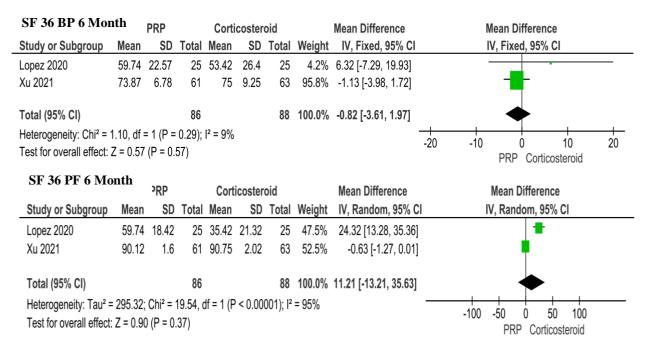


Figure 4 Forest plot of SF36 bodily pain and physical function 6 months

DISCUSSION

The processed liquid portion of autologous peripheral blood with a platelet concentration above the background is known as autologous platelet-rich plasma (PRP). There is a lot of interest in the possibility of autologous **PRP** in regenerative medicine because PRP therapies have been used for a variety of purposes for more than 30 years. ¹⁵ The underlying scientific theory behind PRP therapy holds that the injection of concentrated platelets at the site of injury may begin tissue repair by releasing a variety of biologically active factors (growth factors, cytokines, lysosomes, adhesion proteins) that are in charge of starting the hemostatic cascade,

producing new connective tissue, and revascularizing.

The primary benefits of PRP are its safety and the clever preparation methods utilized by modern commercial machines to create a biologic with a wide range of application possibilities. In contrast routinely used to corticosteroids, PRP is an autologous substance with known side no effects. 16,17,18

As a result of lowering nerve root inflammation, obstructing afferent C fiber nociception, and regulating proinflammatory mediators and phospholipase A2 activity, steroids have analgesic effects.¹⁹

Our study found no significant difference between the PRP and steroid



groups in reducing pain. Many pro- and anti-inflammatory mediators are released by activated platelets, which are good at causing pain but also good at reducing inflammation and discomfort.

By using a variety of intricate pathways connected to anabolic and catabolic cell proliferation, processes, differentiation, and stem cell control, the usual platelet dynamics of PRP affect the milieu prior to tissue repair and regeneration once they have been applied. PRP applications have been implemented in a variety of clinical pathological situations that are typically linked to chronic pain (such as sports injuries, orthopedic pathologies, spinal disorders, and complex chronic wounds), **PRP** thanks to these properties. 20

PRP has the advantage of decreasing pain while also having a regenerative effect that heals tissue damage. PRP preparations are used in precision regenerative medicine therapies to deliver biomolecules that are released by highly concentrated platelet populations that have been activated at the sites of the target tissue.

Consequently, a number of cascades are started that support localized immunomodulation, inflammatory processes, and angiogenesis to aid in

healing and tissue repair. ²¹

Our findings suggest that PRP is as effective as steroid injection for pain reduction in disc herniation, consistent with previous trials by Cameron et al. and Bise et al., which reported significant VAS improvement in both groups.

Functional scores (Oswestry Disability Index, ODI) were compared in two studies. The data showed no significant difference in ODI in the PRP group compared with the steroid group of patients. The Cemeron study also reported the effectiveness of PRP in HNP treatment, with an improvement in VAS of up to 77% and ODI of 8.7% in the 8-year follow-up. ⁷

Patients treated with PRP showed significant improvement in VAS, ODI, and other functional scores. 22 In a nonrandomized comparative trial conducted by Bise et al. in 2020 on 60 patients with lumbar radicular pain, it was discovered that CT-guided epidural PRP injection therapy significantly reduced pain and improved function as measured by the Oswestry disability index (ODI) and the numerical rating scale (NRS). Six weeks after the PRP injection, the results persisted without any issues being noted. ²³

PRP could have a regenerative effect



that leads to preventing disability in HNP patients due its to antiinflammatory qualities and capacity to accelerate the processes of endogenous healing by providing high concentration of growth factors and cytokines. PRP has become widely employed in the treatment musculoskeletal ailments in recent vears. 24 The granules of platelets contain these growth factors, which include vascular endothelial growth factor (VEGF), transforming growth factor 1 (TGF-1), platelet-derived growth factor (PDGF), and insulin-like growth factor 1 (IGF-1). ^{24,25,26}

Within 10 minutes of PRP injection, the platelets clump and coagulate in the desired location, and within an hour, over 95% of the granule load is released. ⁶ Studies have demonstrated that these growth factors are successful in increasing angiogenesis, proliferation, and the production of extracellular matrix proteins. ²⁴ As a result, the main justification for using PRP is to raise the platelet concentration in the targeted areas so that cytokines and GFs may be produced. As a result, this will make it possible to control inflammatory and immunological reactions that lead to tissue repair. 6

We found that SF36 bodily pain after 6

months was not significantly different from the steroid group. Using autologous conditioned serum injections into the lumbar epidural space, Kumar et al. discovered a treatment for radicular discomfort in the lower back that is bothersome. 27 However, in SF36 physical function at 6 months, there is no significant difference. In a study, unsuccessfully after trying conventional conservative techniques in the spine division of a physical medicine and rehabilitation clinic, a sizable of with percentage patients radiculopathy desired alternative nonsurgical therapies.

Thirty of these patients had caudal or lumbar transforaminal epidural PRP therapy, with volumes ranging from 2–3 cc into the foramen to 6–8 cc into the caudal canal. There were no issues, and pain levels rose. ⁶ This explains why PRP therapy and steroid usage have an equivalent impact on lowering patient pain in HNP.

The two most common side effects of epidural steroid injections are known to be hematomas and infection. ^{28, 29} Since PRP is created from the patient's own blood and because platelets contain antibacterial proteins, this makes autologous PRP a potentially safer alternative with reduced risks of



infection and allergies. ³⁰ Furthermore, transforaminal PRP injections might help patients avoid the systemic adverse effects of steroids. ³¹

PRP treatment has a problematic relationship with cost and availability in some healthcare centers. For example, in low- and middle-income countries (LMIC), PRP treatment may have a higher cost compared with steroid treatment. On the one hand, PRP is said to cost almost twice as much in Europe as steroid therapy does. ³² So there is still an available option, and it is widely used for treating HNP patients.

The limitation of this study was the lack of data for the parameter imaging modality to evaluate regenerative structural outcomes objectively. It could be further explored in future studies.

CONCLUSION

This meta-analysis demonstrated no significant difference in pain reduction between PRP and steroid injection for disc herniation. PRP offers comparable analgesic benefits with potential regenerative properties. Further studies should include imaging or biomarker outcomes to assess structural regeneration.

CONFLICT OF INTEREST

There is no conflict of interests and funding.

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