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Literature Review

Platelet-Rich Plasma Treatment for the Lumbar Spine: A Review and Discussion of Existing Gaps

Ji-Eun Irene Yum, BS[1], Arthur J. De Luigi, DO[2], Gregory L. Umphrey, MD[2], Bryan K. Ganter, MD[2], and Min Yoo, MD[2]

From: [1]Mayo Clinic Alix School of Medicine, Rochester, MN; [2]Mayo Clinic, Scottsdale, AZ

Address Correspondence:
Min Yoo , MD
Mayo Clinic Arizona
Scottsdale, AZ
E-mail: yoo.min@mayo.edu

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Background: Platelet-rich plasma (PRP) is obtained by centrifuging autologous whole blood to extract a layer concentrated with platelets, growth factors found in platelet granules, and cytokines. These components work together to promote and facilitate the healing process at sites of injury. An increasing number of clinical studies are assessing the efficacy of PRP as a treatment for lower back pain.

Objectives: Lumbar back pain is a significant cause of years lived with disability. This paper conducts a thorough review of clinical studies on intradiscal, facet-joint, epidural, and mixed-target PRP interventions in the lumbar spine. Furthermore, gaps in the current literature regarding lumbar spinal PRP injections are identified to help guide future clinical trials.

Study Design: Literature review.

Methods: An initial search was conducted using Ovid MEDLINE, focusing on PRP injections in the spine. Boolean operators were used to combine MeSH terms and key words such as "spine," "lumbar spine," "thoracic spine," "cervical spine," "intervertebral disc," "platelet-rich plasma," and "inject." The search revealed an absence of papers about PRP injections into the cervical and thoracic spine, so the review was written with a specific focus on the lumbar spine. For the purposes of this paper, the selected manuscripts were separated into categories of intradiscal, facet-joint, epidural, and mixed-target PRP injections.

Results: A multitude of case reports, case series, prospective clinical studies, and randomized controlled trials have yielded results supporting the use of intradiscal, facet-joint, and epidural PRP injections in the lumbar spine. However, a handful of papers suggest that PRP lacks efficacy in improving lumbar back pain and function. With the relative dearth of literature assessing the effects of spinal PRP injections, additional double-blinded randomized trials are needed. Important findings from available studies include the observation of PRP's increased efficacy over time, the correlation of the number of targeted injection sites with the efficacy of PRP injections, and the correlation of platelet count with PRP injections' efficacy.

Limitations: There exists wide variability in PRP preparation protocols and in the methods of assessing PRP's therapeutic benefits between each study that evaluates PRP's effects in the lumbar spine.

Conclusions: All clinical studies evaluating PRP as a form of treatment for the lumbar spine should include full transparency and details about the methods used for PRP preparation and injection. Future double-blinded randomized trials can fill in existing gaps by assessing the effects of platelet concentration and dose on the extent of clinical improvement as well as by establishing an expected timeline for clinical improvement after PRP injections. Cross-study standardization of which pain scoring systems to utilize for study evaluation would increase comparability among different papers.

Key words: Platelet-rich plasma, lumbar spine, chronic pain, regenerative medicine

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Platelet-rich plasma (PRP) is created by centrifuging autologous whole blood to obtain a layer concentrated with platelets, growth factors found in platelet granules, and cytokines. The purpose of PRP injections is to use the release of these growth factors and cytokines to promote and facilitate the healing process at sites of injury. PRP-derived growth factors include transforming growth factor-beta (TGF-β), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF). Some of these growth factors, including TGF-β, VEGF, and bFGF, can restore angiogenic activity in areas with otherwise poor vascularization, such as the nucleus pulposus, thereby prompting faster repair. Initially, the cytokines in PRP may enable the process of "reparative inflammation" by stimulating fibroblasts, which further secrete their own set of cytokines to recruit and activate macrophages that aid in tissue reconstruction. PRP also includes cytokines that can shift the tissue microenvironment to an anti-inflammatory state, which can allow for the resolution of wound-healing processes (1). A classification system proposed by Ehrenfest et al describes 4 different PRP compositions: 1) pure PRP, 2) leukocyte and PRP, 3) pure platelet-rich fibrin, and 4) leukocyte and platelet-rich fibrin (2). Studies have suggested that the presence of leukocytes can variably influence the efficacy of PRP treatments. Furthermore, specific subtypes of leukocyte, including neutrophils, monocytes, lymphocytes, basophils, and eosinophils, are thought to have differing influences on immune modulation and on tissue repair and regeneration (3-5).

Objective

Utilizing PRP Injections for Lower Back Pain

PRP has a wide breadth of clinical applications, with indications for many dermatologic and orthopedic conditions. This paper will focus specifically on the existing clinical studies regarding the efficacy of different types of PRP injections for the lumbar spine. PRP can be a treatment option for degenerative diseases of the spine because of its regenerative potential, which comes from the stimulation of wound-healing processes and modulation of inflammatory cascades (3). A comprehensive understanding of PRP's effects on lumbar-spine-mediated pain is crucial, since low back pain is the main cause of years lived with disability. Eight hundred forty-three million prevalent cases of low back pain are projected to present themselves globally by 2050 (6). A meta-analysis of studies utilizing animal models has shown that PRP is effective in restoring intervertebral disc height and reducing histological degeneration grades in rabbits and rats (7). More importantly, a plethora of case reports, prospective clinical studies, and randomized controlled trials have been published concerning PRP. This paper will contribute to the existing literature with a detailed review of studies on intradiscal, facet-joint, and epidural interventions in the lumbar spine, followed by an identification of gaps in the current literature with the goal of guiding future trials.

Methods

An initial search was conducted using Ovid MEDLINE, focusing on PRP injections throughout the spine. Boolean operators were used to combine MeSH terms and key words: [(spine or "spine") OR (lumbar vertebrae or "lumbar spine") OR (thoracic vertebrae or "thoracic spine") OR (cervical vertebrae or "cervical spine") OR (intervertebral disc or "intervertebral disc")] AND [platelet-rich plasma or ("prp" or "platelet-rich plasma" or "platelet rich plasma")] AND "inject*." The search was limited to the English language and to human studies.

This query revealed an absence of papers about PRP injections in the cervical and thoracic spine, so the review was written with a focus on the lumbar spine only. Primary research articles describing case reports, case series, prospective clinical studies, and randomized controlled trials were included in the initial search; other papers, such as review articles or in vitro studies, were excluded. Additionally, relevant papers that were referenced within journal articles found in the search were included in this review.

The selected manuscripts were separated into categories of intradiscal, facet-joint, epidural, and mixed-target PRP injections for the purposes of this paper.

Results

Lumbar Intradiscal PRP Injection (Tables 1.1 – 1.3)

Case Reports and Series

Kawabata et al published a report of 2 patients with type I Modic changes who received lumbar intradiscal leukocyte-rich PRP injections. Both patients' scores on the Oswestry Disability Index (ODI) and Roland-Morris

Disability Questionnaire (RMDQ) improved over 6 months, and the visual analog scale (VAS) score improved in one of the 2 patients. In addition, follow-up MRI screenings showed a decrease in signal intensity on the T2-weighted image (T2WI) from the MRI screenings taken before PRP administration, suggesting reductions in inflammation. However, no statistical analysis was performed to assess the significance of the ODI, RMDQ, and VAS changes (8). Another case report of a lumbar intradiscal PRP injection (9) involved a patient with axial low back pain that persisted for one year. Baseline MRI showed reduced T2 nuclear signal intensity, obscuration of the normal horizontal intranuclear cleft, and crescentic fissure in the outer annulus at the L4-L5 disc. Similar moderate decreases in disc height and endplate degeneration appeared with type I Modic changes at the L5-S1 disc. Follow-up MRI at one year showed the efficacy of the PRP injection: the L4-L5 level had increased nuclear signal intensity and normal horizontal intranuclear cleft, while the L5-S1 level showed increased nuclear signal intensity and a reduction of type I Modic changes. Therefore, a positive effect of

Table 1.1. *Intradiscal.*

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	"Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)"	Activated/ Not Activated	Results
"Kawabata, Jan 2023 (8)"	Case report	Intradiscal	PRP injection in 2 patients with Modic change type 1.	"VAS, ODI, RDQ at baseline and 6 months MRI fat suppressed T2WI high signal volume and PDFF at baseline and 6 months"	PS III system (Zimmer Biomet, Warsaw, IN, USA)	"Case1: 50.8 x 10^7 Case 2: 94.4 x 10^7"		"LR-PRP Case1: 12.9 x 10^6 Case2: 17.8 x 10^6"		"ODI and RDQ improved for both cases. VAS only improved in Case 2. Noted decrease in fat suppressed T2WI high signal volume alongside increase in PDFF for both cases."
"Zhang, Oct 2022 (14)"	Prospective clinical study	Intradiscal	"PRP in 31 patients with intervertebral disc degeneration. No control group."	Current/ Best/ Worst NRS, FRI, SF-36 pain and physical function at 0, 1, 4, 12, 24, 48 weeks	Commercial kit - Regen Laboratories SA Inc., Switzerland	1025.3 (± 929.6) x 10^6	1-3	"LP-PRP 7.2 (± 2.1) x 10^6"		"“Success”: meeting the minimal clinically important difference (MCID) for both pain and function without needing surgery. MCID of the FRI, NRS, SF-36 physical function, and SF-36 pain scores defined as a change of 9 points, 2 points, 4.9 points, and 10 points respectively; “Failure”: either needing surgery or not meeting the MCID for pain or function. 71% of 31 patients = success; 29% = failure at 48 weeks. Patients who had multiple levels injected were significantly more likely to result in failure to improve after treatment."

Table 1.1 cont. *Intradiscal.*

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	"Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)"	Activated/ Not Activated	Results
"Lutz, March 2022 (35)"	Retrospective cohort study	Intradiscal	37 patients receiving intradiscal 10x PRP (treatment group) retrospectively compared to a historical cohort (control group) of 29 patients who received <5x PRP (Tuakli-Wosornu 2016)	NRS, FRI, satisfaction with procedure	Emcyte PurePRP II kit		~10			"10x PRP cohort: Success: >= 2 point change in NRS pain score, >= 9 point change in FRI, and satisfaction with the procedure Satisfaction with the procedure: "The procedure met my expectations" or "I improved less than I hoped, but I would undergo the same procedure again for the same results." Success = 26 patients (70%). 7 patients did not meet any of the criteria for success and failed to improve at all. ---------- Comparison to the <5x PRP cohort: Compared to the historical (<5x PRP) cohort, the >10x PRP cohort had significantly greater improvement in both pain and function. Satisfaction rate was also significantly higher in the 10x PRP cohort."
"Schepers, March 2022 (22)"	Prospective single blinded randomized controlled study	Intradiscal	"89 patients with chronic low back pain: 44 in PRP group and 45 in control group (saline injection)."	"Primary outcome measure: NRS and RMDQ; Secondary outcome measures: Mental and physical health SF-12 Measurements at baseline, 1 week, 4 weeks, 2, 4, 6, 9 months"	Harvest Technologies Smartprep2	Assumed kit yield - 1.5 x 10^9		1% WBCs		"Minimally clinical significant change = 2 points on NRS scale, 3 points on RMDQ. No significant differences found in primary and secondary outcome measures between the PRP and control groups."

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Table 1.2. *Intradiscal (part 2).*

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)	Activated/ Not Activated	Results
Akeda, Jan 2022 (20)	Randomized double blinded controlled clinical study	Intradiscal	16 patients with chronic low back pain: 9 in PRP group and 7 in corticosteroid group.	VAS, ODI, RMDQ, JOABPEQ (Japanese Orthopaedic Association Back Pain Evaluation Questionnaire) at 4 and 8 weeks after the initial injection + 4, 8, 12, 26, and 52 weeks after the second optional injection (= 12, 16, 20, 34, 60 weeks after initial injection)	Refer to Akeda 2017	1095.2 ± 362.9 x 10^6	1-3	0.11 ± 0.14 x 10^6 (classified as "Pure PRP" = LP-PRP)	Refer to Akeda 2017	Success was defined as: Improvement of VAS by more than 30% from baseline + improvement in ODI by more than 30% from baseline + no additional treatment + no serious adverse events following injections. At week 8, the success rate of the PRPr group was 55.6%, while that of the CS group was 28.6%. At week 60, the success rate of the PRPr group was 87.5%, while that of the CS group was 40%. These differences were not statistically significant. Retrospective analysis showed that the number of targeted discs and presence of posterior high intensity zones at baseline were significantly but negatively associated with treatment outcomes (Akeda 2023).
Zielinski, Jan 2022 (23)	Randomized double blinded controlled multicenter clinical study	Intradiscal	26 patients with low back pain: 18 in PRP group and 8 in saline control group.	VAS and NPRS at baseline and 8 weeks after injection	Emcyte Pure PRP kit + BioRich Medical ProPlaz Protein Plasma Concentrator filter			LP-PRP		Study terminated after a planned futility analysis. Clinically significant pain relief (30% reduction in both ODI and NPRS) was seen in less than 30% of patients in both PRP and control groups.

Table 1.2 cont. *Intradiscal (part 2)*.

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/mL)	Activated/ Not Activated	Results
Jain, Aug 2020 (36)	Prospective single arm interventional study	Intradiscal	PRP in 20 patients with discogenic low back pain. No control group.	NRS, ODI	Dr PRP USA LLC kit	524.95 +/- 232 x 10^6	1-1	LR-PRP	0.1 mL 10% calcium chloride mixed with PRP	Reduction in both mean NRS scores and ODI scores were statistically significant at 3 months and 6 months. Pearson correlation coefficients between platelet concentration and reduction in NRS/ ODI scores were found to positively correlate with statistical significance.
Navani, May 2018 (11)	Case series	Intradiscal	PRP or BMAC in 20 patients with chronic discogenic lumbar back pain. No control group.	VPS (verbal pain scale), SF-36 at 1, 3, 6, 12, 18 months after treatment	Emcyte Pure PRP Kit				Not activated	On average, patients who received PRP injections improved by >50% in their VPS scores.

PRP treatment appeared through imaging in the case reports by Kawabata et al (8) and Lutz et al (9).

A review article by Monfett et al included a case example describing a patient with chronic lower back pain and left L4 radicular pain. This patient had sustained improvements in Numeric Rating Scale (NRS), Functional Rating Index (FRI), and 36-item Short Form Survey (SF-36) scores in pain and physical function 18 weeks after an intradiscal PRP injection into the L4-5 disc following a positive provocative discography (10). Navani et al published a case series of 20 patients with chronic discogenic lumbar back pain refractory to conservative treatments, including physical therapy (PT), NSAIDs, opioids, muscle relaxants, anti-neuropathic agents, and lumbar epidural steroid injections. Patients were treated with intradiscal injections of either PRP or bone marrow aspirate concentrate (BMAC) (11). PRP was used for patients with normal discs or mildly degenerative discs with disc disruption, whereas BMAC was used for patients with degenerated discs of Pfirrmann index 3 and 4. Pfirrmann index 3 means the disc is inhomogeneous and intermediately gray with an unclear distinction between the nucleus and annulus as well as a normal or slightly increased disc height. Pfirrmann index 4 means that the disc is inhomogeneous and hypointensely dark gray with a loss of distinction between the nucleus and annulus as well as a normal to moderately decreased disc height (12,13). Most of the results section did not distinguish patients who received the PRP injections from those who received the BMAC injections, so it was difficult to tell the statistical and clinical significance of the 2 different substances. Ninety-four percent (17/18) of patients reported > 50% relief in VPS scores at 6 months, which was also maintained in 93% of

Table 1.2 cont. *Intradiscal (part 2)*.

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)	Activated/ Not Activated	Results
Akeda, June 2017 (15)	Prospective clinical study	Intradiscal	PRP in 14 patients with chronic low back pain. No control group.	VAS, RMDQ, neurological assessment (motor strength, sensory function, reflexes) recorded at baseline, 4, 8, 16, 24, 32, 40, 48 weeks after treatment	Sterile blood collection bag system (KARMI Blood Bag, Kawasumi Laboratories) *Used PRPr rather than PRP	907.1±1,039.3 x 10^6	1-2	LP-PRP	Autologous serum and 2% calcium chloride mixed with PRP - centrifuged after incubation to obtain only PRPr (supernatant)	Mean VAS pain score and RMDQ score significantly decreased after injection of PRP releasate at all time points in comparison to baseline. Lumbar lateral radiographs showed no significant progression of disc height narrowing from baseline. MRI showed no significant changes in normalized T2 values of the nucleus pulposus and annulus fibrosus from baseline. Long-term follow up (for 11/14 patients) at an average of 5.9 years after injection showed statistically and clinically significant improvements from baseline in VAS and RMDQ. However, the radiographic measurement of disc height in PRPr injected discs showed a 13.8% decrease compared to baseline (Akeda 2022).

Table 1.3. *Intradiscal (part 3).*

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/mL)	Activated/ Not Activated	Results
Lutz, Jan 2017 (9)	Case report	Intradiscal	PRP in patient with axial low back pain that persisted for one year and was worse upon running. Baseline MRI: L4-5: disc degeneration, crescentic fissure in outer annulus, reduced T2 nuclear signal intensity, obscuration of the normal horizontal intranuclear cleft. L5-S1: disc degeneration, moderate decreased disc height, mild/moderate endplate degeneration associated with type I Modic changes.	MRI at baseline and at 1 year post injection	Arteriocyte Magellan Autologous Platelet Separator (Hopkinton, MA, USA)		1-19			Follow-up MRI at 1 year showed: L4-L5: increased T2 nuclear signal intensity, normal horizontal intranuclear cleft, no change in crescentic fissure in outer annulus. L5-S1: increased T2 nuclear signal intensity, reduction of type I Modic changes compared with the pre-injection MRI.

patients at 18 months (14/15). Unfortunately, it appears that no subgroup analysis was performed specifically for the PRP treatment group. Overall, while these reports suggest the potential benefits of intradiscal PRP, there are inherent limitations in the case reports and series.

Single-Arm Clinical Trials

A recent single-arm clinical trial treated 31 participants with low back pain that was discogenic in nature, as suggested by the MRI findings and provocation of concordant pain by the discography, with intradiscal PRP injections (14). Of the patients, 71% were reported to have experienced successful results, defined as meeting the minimal clinically important difference (MCID) for improvement in pain and function measured by the NRS, FRI, and SF-36. These improvements were sustained throughout the 4-, 12-, 24-, and 48-week time points. Similarly, in another preliminary prospective clinical study, 14 patients with chronic low back pain thought to be discogenic based on clinical presentation (low back pain without leg pain), MRI, and provocative discography, were injected with PRP releasate (PRPr) (15). PRPr is the serum fraction that includes bioactive proteins, isolated from exogenously activated platelets. Mean VAS pain scores and RMDQ scores were observed to have improved significantly at 4 weeks, and this improvement was sustained at 48 weeks. On the other hand, there were no significant changes in lumbar lateral radiograph images of disc height or in the T2 values of MRI images of the nucleus pulposus and annulus fibrosus at 48 weeks post-injection. Furthermore, long-term follow-up 5.9 years after the injection demonstrated that radiographic measurement of disc height in PRP-injected discs actually showed a 13.8% decrease compared to the baseline, even though patients had significant improvements from their baseline VAS and RMDQ scores (16). There is an interesting disconnect here between the improved pain/function scoring systems and the imaging results that suggest PRPr injection may not induce structural restoration of degenerated intervertebral discs.

An older prospective clinical trial involved 22 patients with low back pain who received PRP injections in one to 5 lumbar discs (17). Provocative discography and MRI, while utilized for patient selection, were not required criteria, and the patients could be selected based on clinical features alone.

Table 1.3 cont. *Intradiscal (part 3)*.

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)	Activated/ Not Activated	Results
Tuakli-Wosornu, Jan 2016 (18)	Prospective, double-blinded, randomized controlled study	Intradiscal	Patients had chronic lumbar discogenic pain: 29 patients in PRP group and 18 patients in control contrast agent group.	NRS, FRI, SF-36 pain and physical function at 0, 1, 4, 8 weeks, 6 months, 1 year post injection NASS at 1, 4, 8 weeks, 6 months, 1 year post injection	Harvest Technologies Corporation (Plymouth, Massachusetts)		3-5 (Cheng 2019)			Statistically significant improvements in NRS Best pain, FRI, and NASS satisfaction between the treatment and control groups over 8 weeks. No significant improvement in NRS current and worst pain, SF-36 physical functioning/pain. Longitudinal analysis was only done for the PRP group. Statistically significant improvement in NRS Worst Pain, FRI, SF-36 Pain at 6 mo. Statistically significant improvement in NRS Worst Pain, FRI, SF-36 Pain/ Physical Function at 1 yr. Statistically significant improvement was sustained at 2 years for NRS Worst pain, FRI, SF-36 Pain/Function (Monfett 2016). Statistically and clinically significant improvement in NRS, SF-36 Pain/ Function, and FRI at 5-9 years post injection (for the 19/29 patients that completed the 5-9 year follow up survey). NASS showed that 58% of treated patients expressed satisfaction (Cheng 2019).

Table 1.3 cont. *Intradiscal (part 3)*.

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)	Activated/ Not Activated	Results
Monfett, April 2016 (10)	Case Report (in review paper)	Intradiscal	PRP in patient with chronic lower back pain and left L4 radicular pain from a small, left foraminal disc protrusion.	NRS, FRI, SF-36 pain and physical function at 18 weeks post-procedure						Sustained improvements in NRS, FRI, SF-36 Pain and Physical function.
Levi, Dec 2015 (17)	Prospective Clinical Study	Intradiscal	PRP in 22 patients with intradiscal low back pain. No control group.	VAS, ODI at baseline, 1, 2, 6 months	Harvest Technologies Smartprep 2			LR-PRP		Success was defined as 50% improvement in VAS with 30% improvement in ODI. At 1 month follow up: 14% of patients had success. At 6 month follow up, 47% of patients had success.

Medial branch blocks and sacroiliac joint injections were performed for non-midline pain to rule out alternative etiologies of pain. With success being defined as a respective > 50% and > 30% improvement in the VAS and ODI score, a corresponding 14% and 47% of patients had success at one-month and 6-month follow-ups. Interpretation of these single-arm clinical trials is limited by the lack of control groups.

Randomized Controlled Studies

A prospective, double-blinded, randomized controlled trial enrolled 47 patients with chronic low back pain. This study implemented intradiscal PRP injections following provocative discography in the treatment group and additional contrast injections after discography in the control group. Inclusion criteria consisted of positive provocative discography and the presence of a grade 3 or 4 annular fissure, while patients with a grade 5 annular fissure or spinal stenosis were excluded (18). The results showed statistically significant improvements in the treatment group's NRS best pain, FRI, and North American Spine Society (NASS) satisfaction indexes compared to the control group's at 8 weeks post-treatment. However, no statistically significant improvement was shown in the NRS current and worst pain or in the SF-36 pain and physical function scores. Although longitudinal analysis of only the PRP treatment group showed statistically significant improvements in the NRS worst pain, FRI, and SF-36 pain and physical function scores at one year, the PRP treatment group was not compared to the control group after 8 weeks. These improvements were sustained when patients were evaluated at 2 years post-injection (10) as well as at the 5-9-year mark (19). More recently, a prospective, double-blinded, randomized controlled study was conducted, utilizing PRPr rather than PRP (20). This study included 16 patients with lower discogenic back pain that was confirmed with provocative discography and MRI evidence of the degeneration of at least one lumbar disc. Nine patients were assigned to receive intradiscal PRPr injections, and 7 were assigned to receive intradiscal corticosteroid (CS) injections (2 mg betamethasone sodium phosphate). At the primary endpoint of 8 weeks post-injection, patients of both groups were offered an additional PRPr injection, which most patients accepted. Mean VAS and RMDQ scores decreased significantly in both the PRPr group and CS group at all time points in comparison to the baseline; however, the differences between the 2

groups were not statistically significant. In this study, success was defined as improvement of both VAS and ODI scores by more than 30% from the baseline, with no additional treatments and no serious adverse events from the injection. At week 8, the PRPr group's success rate was 55.6%, while the CS group's was 28.6%. At week 60, the success rate of the PRPr group was 87.5%, while that of the CS group was 40%. Again, none of these differences were statistically significant. These results could possibly be attributed to the small sample size and subsequent lack of power for statistical analysis. These results suggest that PRP injections may be at least as effective as, if not more effective than, corticosteroid injections. Lastly, it is notable that a retrospective analysis of this study showed that the presence of posterior high intensity zones at the baseline were negatively associated with treatment efficacy (21).

In contrast, a prospective, single-blinded, randomized controlled study by Scheper et al used either intradiscal PRP or saline injections to treat patients with chronic lower back pain (22). Of the 98 randomized patients, 89 patients with complete outcome data were analyzed. No significant differences between the PRP and control groups were observed in the outcome measures of the physical and mental health scores on the NRS, RMDQ, or SF-12. Interestingly, this study excluded patients with Modic changes shown in MRI, citing another study that suggested Modic changes were related to low-grade infections, and instead relied only on positive provocative discography as the inclusion criteria. However, during the PRP injections, no contrast was administered to confirm intradiscal placement, because of a concern that a contrast medium could decrease the efficacy of PRP. Reliance on discography without contrast and the exclusion of patients with Modic changes likely decreased the accuracy of the diagnoses of discogenic pain. Lastly, a prospective, multicenter, double-blinded, randomized controlled trial assigned 26 patients with discogenic lumbar pain diagnosed by MRI and discography to either the intradiscal PRP group or the intradiscal saline control group (23). Clinically significant pain relief (as defined by 30% reduction in both ODI and Numeric Pain Rating Scale [NPRS] scores) was seen in under 30% of patients in both the PRP and control groups at 8 weeks, and the study was terminated after a planned futility analysis from the 26 patients, even though 60 patients were originally planned to be included in the study. The relatively short outcome follow-up period is a limitation of this study.

Lumbar Facet Joint PRP Injection (Table 2)

Fewer studies of lumbar facet-joint PRP injections exist. A single-arm clinical trial treated 19 patients who had lumbar facet joint syndrome with intraarticular facet joint PRP injections under fluoroscopic guidance (24). VAS, RMDQ, ODI, and modified MacNab criteria were measured at the baseline, immediately after the injection, and at one week and at one, 2, and 3 months post-injection. Significant decreases in VAS and ODI scores were observed starting from one week after treatment, while reduced RMDQ scores were seen immediately after treatment. These improvements were maintained at the 3-month mark. With the MacNab criteria, 43.37% of patients were "excellent" or "good" at the baseline, and at 3 months, 78.95% were "excellent" or "good." That significant improvements were noted from only one week after the procedures is rather surprising and atypical of PRP injections for musculoskeletal conditions, but the lack of a control group could have meant a significant placebo response.

The same group of authors subsequently performed a prospective, randomized, controlled study of 46 patients with lumbar facet joint syndrome (25). These patients were randomized to receive either intraarticular lumbar facet joint LP-PRP (leukocyte-poor) injections (0.5 mL PRP per joint) or corticosteroid (0.5% lidocaine and 5 mg/mL betamethasone at a 4:1 ratio with 0.5 mL total volume) injections. Each patient needed positive diagnostic intraarticular facet joint blocks with local anesthetics before proceeding with the study. Most patients received treatment in multiple facet joints. VAS, RMDQ, ODI, and modified MacNab criteria were measured at the baseline, immediately after injection, and at one week and one, 2, 3, and 6 months after injection. Significant improvements in VAS, RMDQ, and ODI scores were found for both treatment groups through to 6 months. While these improvements were significantly greater for the corticosteroid group at one month, the improvements were greater for the PRP group at 3 and 6 months. As for the MacNab criteria, at 6 months after treatment, patients who had a PRP injection were significantly more likely to report treatment satisfaction than those who had a corticosteroid injection. These results suggest that while PRP takes longer to provide symptomatic relief, the substance may eventually provide a greater duration of benefits than do corticosteroid injections.

Lumbar Epidural PRP Injection (Table 3)

There are several single-arm and randomized

Table 2. *Facet joint*.

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)	Activated/ Not Activated	Results
Wu, Sept 2017 (25)	Prospective, randomized, controlled study	Facet joint (multiple levels)	46 patients with lumbar facet joint syndrome: 23 in group A (PRP) and 23 in group B (0.5% lidocaine and 5 mg/mL betamethasone - 4:1).	VAS (at rest and during flexion), RMDQ, ODI, and modified MacNab criteria at baseline, immediately after injection, 1 week, and 1, 2, 3, and 6 months	Non-commercial double spin PRP	100-300 x 10^9	4-5	LP-PRP		Significant decrease in VAS at rest and during flexion, RMDQ, and ODI through to 6 months for both groups. The decrease was significantly greater for group B at 1 week and at 1 month but significantly greater for group A at 3 months and beyond for all scoring systems. MacNab criteria: At 6 months, group A was significantly more likely to report treatment satisfaction than group B.
Wu, Nov 2016 (24)	Prospective clinical study	Facet joint (multiple levels)	PRP for 19 patients with lumbar facet joint syndrome. No control group.	VAS (at rest and during flexion), RMDQ, ODI, and modified MacNab criteria at baseline, immediately after injection, 1 week, and 1, 2, and 3 months	Non-commercial double spin PRP	100-300 x 10^9	4-5	LP-PRP		Significant decrease in VAS at rest and during flexion, RMDQ, and ODI through to 3 months. MacNab criteria: At baseline, 43.37% of patients were "excellent" or "good." At 3 months, 78.95% were "excellent" or "good."

Table 3. *Epidural.*

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)	Activated/ Not Activated	Results
Wongjarupong, April 2023 (29)	Triple blinded randomized control study	Transforaminal epidural	30 patients with single level lumbar herniated disc: 15 in PRP group and 15 in triamcinolone control group.	LegVAS, BackVAS, ODI at 0, 2, 6, 12, 24 weeks	Non-commercial double spin PRP	>= 1 x 10^6	2.86 ± 0.85	12,610±4202 (Lymphocyte dominant at 75.35 ± 5.92%)		Statistically and clinically significant reduction in LegVAS seen at 6, 12, and 24 weeks in PRP group vs triamcinolone group.
Le, Jan 2023 (27)	Prospective clinical study	Transforaminal epidural	PRP for 25 patients with lumbar disc herniation at L4/ L5 or L5/S1 with radicular pain. No control group.	VAS, ODI, SLRT at baseline, 1 week and at 1, 3, 6, and 12 months	Non-commercial double spin PRP					Statistically significant improvement in VAS score at 1 week, maintained at 1 year follow up. ODI improved in >50% of patients after 1 year, and the percentage of "crippled" patients went from 76% to 0%. Increased percentage of negative SLRT at 1 year.
Ruiz-Lopez, April 2020 (30)	Prospective randomized controlled double-blinded study	Caudal epidural	50 patients with chronic degenerative lumbar spinal pain: 25 in PRP group and 25 in corticosteroid group.	VAS at baseline, 1, 3, 6 months SF-36 at baseline and 6 months	Non-commercial single spin PRP			LR-PRP		Significantly lower VAS scores in the corticosteroid (CS) group vs PRP group at 1 month. Significantly lower VAS scores in the PRP group vs CS group at 3 and 6 months. Significantly greater improvement in multiple SF-36 domains for the PRP group vs CS group.

Table 3 cont. *Epidural*.

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)	Activated/ Not Activated	Results
Bise, Feb 2020 (28)	Descriptive prospective comparative study	Interlaminar epidural	60 patients with unilateral resistant lumbar radicular pain: 30 in PRP group and 30 in corticosteroid group.	NRS, ODI at baseline and at 6 weeks	Non-commercial single spin PRP	520 ± 114 x 10^6	3	LP-PRP 310 ± 293 x 10^3 / mL		Significant decrease in NRS and ODI for both ESI and PRP injection groups. No significant difference in median decrease in NRS and ODI between the two groups.
Bhatia, Sep 2016 (26)	Prospective clinical study	Interlaminar epidural	PRP in 10 patients with lumbar disc herniation/ prolapse in MRI. No control group.	VAS, MODQ, SLRT, neurological examination of lower limb performed at baseline, 3 weeks, and 3 months						The patients had gradual improvement in VAS (most scored <4 at 3 months), MODQ (most scored <30% at 3 months), SLRT (most scored >70 at 3 months).

controlled trials of lumbar epidural PRP injections. A 2016 pilot study enrolled 10 patients who had lumbar disc pathology and corresponding low back pain with or without radiculopathy and treated each patient with 5 mL of an epidural PRP injection using an interlaminar approach (26). The patients had gradual improvements in VAS, MODQ index, and straight leg raise test (SLRT) scores, which were sustained through a 3-month period after the injections. Unfortunately, no analysis was done to assess the statistical significance of the improvements in each measure. There was also a lack of information on how the PRP was prepared. Another more recent single-arm trial treated 25 patients with lumbar disc herniation at the L4/L5 or L5/S1 level and corresponding radicular pain (27). Each patient received a transforaminal epidural PRP injection (4 mL). Statistically significant improvements in VAS scores were seen at one week and maintained through one year. ODI scores improved for more than half of the patients after one year, and the percentage of patients with "cripple" pain (61-80% disability) decreased from 76% to 0%. There was also a statistically significant increase in the number of patients with negative SLRTs.

A nonrandomized comparative study evaluated the therapeutic effects of interlaminar epidural PRP injections (2.5 mL, platelet concentration 520,000/mL ± 114,250) as compared to those of corticosteroid (2.5 mL hydrocortancyl 2.5%) injections in 60 patients with unilateral resistant lumbar radicular pain related to posterolateral disc herniations (28). There was a significant decrease in NRS and ODI scores for both groups at the 6-week mark, with no significant difference between the improvements in each group. Because the patients were not randomized, there was a significant difference in the groups' mean age (corticosteroid group 50, PRP group 59). Additional limitations of this study include a relatively short-term follow-up period (6 weeks) and a lack of documentation of drug therapy and PT during that follow-up period.

A triple-blinded, randomized controlled study published in 2023 attempted to compare the efficacy of epidural PRP injections to

that of epidural steroid injections (29). Thirty patients with unilateral herniated nucleus pulposus corresponding to clinical presentation were assigned to receive a transforaminal epidural injection with either 2 mL PRP + 0.5 mL normal saline or 40 mg triamcinolone + 2 mL one percent lidocaine. A greater number of statistically significant reductions in LegVAS scores, the primary endpoint measurement, were seen in the PRP group than in the corticosteroid group from the 6-24-week post-procedure time point measurements. BackVAS and ODI scores, however, showed no statistically significant differences between the 2 groups. This study suggests that the effects of PRP epidural injections may be comparable or even superior to the effects of corticosteroid injections. Similarly, a prospective, double-blinded, randomized controlled study evenly assigned 50 patients with chronic degenerative lumbar spinal pain to receive either a 20 mL caudal epidural injection of a corticosteroid mixture (60 mg triamcinolone acetonide) or LR-PRP (16.5 mL of PRP) (30). The volume of PRP used in this study is much greater than the volume used in other studies, but neither platelet dose nor concentration factor was stated. The corticosteroid group showed significantly lower VAS scores than did the PRP group at one month, but the improvements in the PRP group's VAS scores surpassed the corticosteroid group's at 3 and 6 months. There was also significantly greater improvement in multiple SF-36 domains for the PRP group than for the corticosteroid group. These results lend further support to claims that PRP injections may take longer to show full efficacy than corticosteroid injections do.

Lumbar Mixed PRP Injection (Table 4)

In some studies, mixtures of several lumbar spine injections were performed on the same patients. An observational retrospective pilot study administered intradiscal, peridural, and facet joint infiltrations together with plasma rich in growth factor (PRGF) to treat 86 patients with a history of chronic lower back pain and lumbar spine degenerative disease (31). VAS scores were shown to improve significantly from the baseline to one to 3 to 6 months. At 6 months, 90.7% of patients showed an "excellent" score of VAS <= 3.

A case series by Barbieri et al described 32 patients with chronic spinal pain of multifactorial origin (32). Each patient received injections of PRGF, a PRP derivative, followed by second injections after 15 days. Multiple areas were injected with PRGF, including the disc, sacroiliac joint, and neuroforamen, based on clinical presentation and response to diagnostic injections. PRGF treatment did not lead to significant improvement of the patients' conditions, as assessed by Patient Global Impression of Change (PGIC), VAS, and ODI measurements at 3 and 6 months. Interestingly, researchers later divided the cohort into responders and nonresponders, with 8 patients in the responder group. These responders showed a clinically relevant improvement in ODI scores at 3 and 6 months post-treatment, a significant decrease in VAS spine scores at 3 and 6 months post-treatment, and a significant decrease in VAS scores 6 months post-treatment. The responder group had younger patients, more men, fewer MSK comorbidities, and less sedentary lifestyles. This study suggests that PRP therapy may not be appropriate for all patients with lower back pain and that identifying the groups of patients who are more likely to respond favorably could be a goal of future trials. There were several limitations in this study, including a lack of platelet concentration/dose analysis, the absence of a control group, and the large variety in treatment target sites depending on patient presentation. Machado et al also published a prospective case series, in which facet-joint, disc, transforaminal epidural, caudal epidural and/or paravertebral-muscle PRP injections were performed for 46 patients with refractory chronic low back pain (33). VAS and RMDQ scores were recorded at the baseline and at 2, 12, 26, and 52 weeks after treatment, and each measurement improved significantly at each time point in comparison to the baseline. Consumption of opioid and nonopioid pain medications was also significantly lower at week 52 than at the baseline, with the number of patients taking opioids going down by 65.7%. Like Barbieri's case series, it is difficult to interpret the clinical implications of this study because of the large variation in pathologies and location of treated sites for each patient.

When PRP is exogenously induced to release alpha granules, the resulting cytokine and growth factor-rich solution is called platelet lysate or platelet releasate. In 2020, Rawson et al published a case report in which 2 patients with symptomatic herniated discs received 2 treatments that each introduced one mL of PRP into both the facet joint and spinal ligament and 3 mL of platelet lysate into the epidural space (34). This case report includes imaging at the baseline and 4 weeks after treatment. Both patients reported overall improvement in pain and function, and both had lumbar MRIs that showed notable resorption of disc herniation. More studies that use imaging as a primary endpoint as well as pain and function scoring systems would be informative additions to the field.

Table 4. *Mixed*.

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/ mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/ mL)	Activated/ Not Activated	Results
Barbieri, Jan 2022 (32)	Case series	Intervertebral, epidural, and/ or facet and sacroiliac Joints	Plasma rich in growth factors (PRGF) in 32 patients with chronic low back pain. No control group.	Patient Global Impression of Change (PGIC), VAS, ODI at 3 and 6 months post-treatment	PRGF-Endoret (PRGF System IV; Biotechnology Institute, Victoria, Spain) Single spin	Baseline: 282.0 ± 67.1 x 10^6 Concentrated: Not measured, estimated to be about 1 x 10^9	Estimated to be 2-3	likely LP-PRP	Activated with 10% CaCl2	No significant changes in overall cohort. When the cohort was divided into responders (Rs) and nonresponders (NRs), there were 8 patients in the R group. These 8 patients showed a clinically relevant improvement in ODI score at 3 and 6 months post treatment, significant decrease in VAS spine at 3 and 6 months post treatment, and significant decrease in VAS 6 months post treatment.
Machado, Jan 2022 (33)	Case series	Facet joint, intervertebral, epidural (foraminal, caudal), muscular	PRP in 46 patients with chronic low back pain. No control group.	VAS, RMDQ at baseline 2, 12, 26, 52 weeks Pain medication form NASS at 52 weeks	Non-commercial double spin PRP: Turn down- Turn up method (Machado 2019)	Estimated to be 749 ± 307 x 10^6	Estimated to be 4.07	likely LR-PRP		Statistically significant lower RMDQ and pain VAS scores at week 2,12, 26, and 52 in comparison to baseline. Consumption of opioid and nonopioid pain medications were significantly less at week 52 in comparison to baseline. Number of patients taking opioids decreased by 65.7%. Exploratory analysis showed that there were lower RMDQ scores for those who received epidural injections than those who did not. Patients who received injections into 3 or more targets had lower RMDQ scores.

Discussion

Increased Efficacy of PRP Observed Over Time

Various studies have suggested that PRP treatments' action in improving symptoms may be delayed. In a study of intradiscal PRP injections into the lumbar spine, 14% of patients achieved "success" in treatment (defined by at least 50% improvement in VAS score + 30% improvement in ODI score) at the one-month follow-up, while 47% of patients achieved "success" at the 6-month follow-up (17). The randomized controlled study by Wu et al comparing lumbar facet-joint PRP injections to corticosteroid injections showed that corticosteroids had a greater impact at one month, while PRP injections began to trump corticosteroids at 3 months (25). Similarly, Ruiz-Lopez et al's randomized controlled study assessing lumbar epidural PRP injections demonstrated a greater improvement in VAS scores in the corticosteroid-treated patient group at one month and a greater improvement in the PRP-treated patient group at 3 and 6 months (30). Finally, an observational retrospective study that used a mix of intradiscal, peridural, and facet-joint PRP injections at the lumbar spine showed that VAS scores decreased significantly more at 6 months than at 3 months or one month after injection (31). While these studies suggest that PRP has a greater efficacy when unveiled at later time points after the procedure, other studies demonstrate quicker patient responses to PRP injections, ranging from as early as one week to 8 weeks post-procedure (15,18,24,27-29,34).

The Correlation of Number of Targeted Injection Sites with Efficacy of PRP Injections

In many of the aforementioned studies, PRP injections were administered to multiple lumbar discs in each patient. Retrospective analysis (21) of Akeda's

Table 4 cont. *Mixed.*

Author (et al.), Date	Type of Study	Type of Injection	Control vs. Treatment Groups	Pain Scoring System & Timepoints (Post - Procedure)	PRP Extraction Method (kits)	Platelet Count in PRP sample (platelets/mL)	Platelet Fold Change from Baseline	Leukocyte Rich (LR) / Leukocyte Poor (LP) (WBCs/mL)	Activated/ Not Activated	Results
Rawson, March 2020 (34)	Case report	Facet joint/ spinal ligament (PRP), interlaminar epidural (platelet lysate)	PRP and PRP lysate (PRPr) in 2 patients with symptomatic herniated lumbar discs.	MRI at baseline and 4 weeks after second treatment	Non-commercial double spin PRP		4-6	LR-PRP	Not activated	Both cases showed resolution of symptoms such as radicular pain and paresthesias upon completion of two treatments. MRI showed resorption of disc herniations.
Kirchner and Anitua, Oct 2016 (31)	Observational retrospective study	Intradiscal, peridural, facet joint	PRP in 86 patients with chronic lower back pain and lumbar spine degenerative disease. No control group.	VAS at baseline and 1, 3, and 6 months	PRGF-Endoret (PRGF System IV; Biotechnology Institute, Victoria, Spain) Single spin		Estimated to be 2	LP-PRP	20 uL of PRGF activator (10% weight/ vol CaCl2) per mL of PRGF	Statistically significant drop in average VAS from baseline to 1 to 3 to 6 months: VAS at baseline (8.4 ± 1.1), and 1 (4.0 ± 2.6), 3 (1.7 ± 2.3), and 6 (0.8 ± 1.7) months. Excellent = 0-3, moderate = 3.1-6.5, ineffective = 6.6-10 At the end point of the study, 90.7% of patients showed an excellent score

2022 randomized controlled study (20) revealed that a greater number of targeted discs was negatively associated with clinical outcome. Similarly, Zhang's 2022 prospective clinical study showed that patients who were injected at multiple levels were likelier to experience failure to improve after the injections (14). The reason for these results is unclear, but the patients who received PRP injections in multiple discs might have had more diffuse lumbar spondylosis, which could have translated to poorer outcomes than in patients with more focal spine pathologies.

However, some multi-site injection case series by Barbieri et al and Machado et al demonstrated the opposite. In Barbieri's study, 46% of patients treated at 2 different sites responded to the procedure, whereas 12% of patients treated at one site responded (32). Similarly, in Machado's study, patients who had 3 or more structures injected showed greater improvement in RMDQ scores (33). Nonetheless, the results from these studies do not necessarily contradict those of the intradiscal PRP studies above, since the difference is between targeting multiple discs and multiple distinct targets in the spine (disc, facet joint, epidural, etc.).

The Correlation of Platelet Count with Efficacy of PRP Injections

Several studies demonstrate platelet count's potential impact on the efficacy of PRP injections. A retrospective cohort study compared 37 patients who received intradiscal injections of PRP concentrations of 10x (from baseline platelet count) to a cohort of 29 patients who received PRP injections of < 5x concentration (35). The lower-concentration PRP group consisted of participants from Tuakli-Wosornu et al's 2016 paper discussed earlier in this review. Compared to the <5x PRP cohort, the 10x PRP cohort had significantly greater improvement in both pain and function, according to the NRS and FRI scores. Patient satisfaction rate was also significantly higher in the 10x PRP cohort. One limitation of this study is that follow-up time points for all patients are different (from 3 to 43 months), since this was a retrospective cohort study. Notably, the 10x PRP cohort had worse baseline pain and function scores and therefore theoretically had greater room for improvements. Like this cohort study, a prospective single-arm interventional study suggested the value of a higher platelet concentration (36). The study included 20 participants with discogenic low back pain who showed a statistically significant improvement in pain and function scores (NRS and ODI) both 3 and 6 months after their PRP injections. Pearson correlation coefficients showed a statistically significant positive correlation between platelet concentration and the reductions seen in NRS and ODI scores. If using higher platelet concentrations and doses has additional benefits, it would be worthwhile for future studies to attempt to assess if those benefits plateau after a certain concentration and dose.

Limitations

The Need for Standardization of PRP Preparation and of Evaluation Methods for PRP Efficacy

One of the biggest challenges in reviewing and analyzing clinical trials that involve PRP is the lack of standardization in protocol. Existing studies have a large amount of variation in PRP preparation protocols and the methods of assessing PRP's efficacy (Tables 1-4).

Variations in PRP preparation protocols include the use of noncommercial in-house protocols rather than commercial kits. Centrifuge spin speeds and time vary significantly in each method. There are also double- or single-spin methods, yielding different PRP products, but studies do not always specify the reasoning behind the choice between a double and a single spin. Few manuscripts provide detailed information on PRP composition, which includes such factors as platelet count, platelet concentration fold change from baseline whole blood, whether the substance is leukocyte poor or rich (more specifically, neutrophil poor or rich and monocyte poor or rich), and whether PRP was activated (Table 1-4). In order to develop a better understanding of what is the most effective PRP composition based on target structures, future studies should include detailed cellar analysis of PRP used for their trials. The acceptance of a standard system for classifying PRP, such as the MARSPILL classification (37), would also allow for increased clarity.

There are a plethora of methods for assessing outcomes after PRP injections, which have been mentioned throughout all the studies synthesized in this review: FRI, MacNab criteria, NASS, NRS/NPRS (best, current, worst pain), ODI/modified ODI, RMDQ, SF-36 domains, and VAS (legVAS, backVAS). A select number of studies also use imaging of the lumbar spine as primary or secondary endpoints (Table 1-4). Standardizing evaluation methods and the definitions of clinically significant improvement would allow for more reliable systemic review and meta-analysis results while reducing potential bias. Increased incorporation of imaging data can

also improve clarity on the regenerative properties of PRP treatments in the lumbar spine.

Conclusions

Various case reports, prospective clinical studies, and randomized controlled trials have results supporting the use of PRP in the lumbar spine. However, some papers' results suggest that PRP lacks efficacy in improving lumbar back pain and function (22,23,32). Compared to existing literature on the use of PRP for the treatment of peripheral joint osteoarthritis and tendinopathies, there is a relative dearth of literature assessing the effects of PRP in the spine. Additional double-blinded randomized trials are warranted, ideally including studies to assess the effects of platelet concentration and dose, to develop a universal protocol for PRP preparation depending on treatment target sites (joint, intradiscal, epidural). Future studies should also attempt to establish an expected timeline for clinical improvement after PRP treatments in the spine. As each of these questions is addressed, there will be more clarity regarding the standardized protocols for and efficacy of PRP treatments for lumbar spine pathologies, and the adoption of PRP in clinical practices could potentially become universal.

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