Efficacy of Platelet-rich Plasma for Low Back Pain: A Systematic Review and Meta-analysis

Zhaopeng Xuan[1] Wenjun Yu[1] Yichen Dou[1] Tao Wang[1]

[1] Department of Hand Surgery, The First Hospital of Jilin University, Changchun, Jilin, China

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Address for correspondence Tao Wang, MD, Department of Hand Surgery, The First Hospital of Jilin University, No. 218 Ziqiang Street, Nanguan District, Changchun, Jilin, P. R. China 130041 (e-mail: w-t585@163.com).

Abstract

Background Platelet-rich plasma (PRP) may be beneficial for patients with low back pain. However, the results remain controversial. We conducted a systematic review and meta-analysis to explore the efficacy of PRP for low back pain.

Methods PubMed, Embase, Web of Science, EBSCO, and Cochrane Library databases were searched systematically. Randomized controlled trials (RCTs) assessing the effect of PRP on low back pain were included. Two investigators independently searched articles, extracted data, and assessed the quality of included studies. The primary outcome was pain scores within 8 weeks. Meta-analysis was performed using the random-effects model.

Results Three RCTs involving 131 patients were included in the meta-analysis. Overall, compared with control intervention for low back pain, PRP injection was found to reduce pain scores significantly (mean difference: -1.47; 95% confidence interval [CI], -2.12 to -0.81; $p < 0.0001$), improve the number of patients with $> 50\%$ pain relief at 3 months (risk ratio [RR]: 4.14; 95% CI, 2.22–7.74; $p < 0.00001$), and offer relatively good patient satisfaction (RR: 1.91; 95% CI, 1.04–3.53; $p = 0.04$). No increase in adverse events was reported after PRP injection (RR: 1.92; 95% CI, 0.94-3.91; $p = 0.07$).

Conclusions Compared with control intervention for low back pain, PRP injection was found to improve pain relief and patient satisfaction significantly with no increase in adverse events.

Keywords
- low back pain
- platelet-rich plasma
- pain scores
- systematic review
- meta-analysis

Introduction

Low back pain is a common and devastating problem for patients and physicians, and it results in high morbidity and a great economic burden.[1–5] Low back pain is the most common cause of disability of patients between 45 and 65 years of age.[6,7] Approximately 20% of patients have a recurrence within 6 months of the initial episode, and some experience chronic symptoms. Numerous factors can cause low back pain including intervertebral disk herniation and lumbar facet joint syndrome.[8–11]

Platelet-rich plasma (PRP) is an autologous biological blood-derived product and can release high concentrations of platelet-derived growth factors to enhance the body's natural healing response.[12,13] PRP also possesses antimicrobial properties and may have some ability to prevent infections.[14,15] Local injection of PRP is reported to be an effective modality to reduce pain, disability, and functional limitation, and to improve structural integrity and biomechanical strength for various painful conditions including tendinopathy, muscle strain injury, ligament injury, and knee osteoarthritis.[16–21] PRP was found to stimulate the metabolism of intervertebral disk cells in vitro and promote a reparative effect on rabbit degenerated intervertebral disks.[22,23] Intra-articular knee injection of PRP results in pain relief and improves knee function and quality of life in younger patients with a low degree of articular degeneration.[24] Previous studies demonstrated that PRP by periarticular injection, sacroiliac joint injection, or intradiskal injection

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results in significant improvement in pain scores for low back pain.[25,26]

In contrast to this promising finding, however, some relevant randomized controlled trials (RCTs) showed that PRP injection had no influence on pain scores and patient satisfaction for low back pain.[27,28] Considering these inconsistent effects, we therefore conducted a systematic review and meta-analysis of RCTs to evaluate the effectiveness of PRP injection in patients with low back pain.

Materials and Methods

This systematic review and meta-analysis were conducted according to the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement[29] and the *Cochrane Handbook for Systematic Reviews of Interventions*.[30] All analyses were based on previous published studies. Thus no ethical approval and patient consent were required.

Literature Search and Selection Criteria

PubMed, Embase, Web of Science, EBSCO, and the Cochrane Library were systematically searched from inception to September 2017, with the following keywords: *platelet-rich plasma* or *PRP,* and *low back pain* or *lumbar pain.* To include additional eligible studies, the reference lists of retrieved studies and relevant reviews were also hand-searched, and the process was performed repeatedly until no further article was identified. Conference abstracts meeting the inclusion criteria were also included.

The inclusion criteria were as follows: study population, patients with low back pain; intervention, platelet-rich plasma; control intervention; outcome measure, pain scores; and study design, RCT.

Data Extraction and Outcome Measures

The following information was extracted for the included RCTs: first author, publication year, sample size, baseline characteristics of patients, PRP, control, study design, pain scores within 8 weeks, $>$ 50% pain relief at 3 months, relatively good patient satisfaction, and adverse events. The author was contacted to acquire the data when necessary.

The primary outcome was pain scores within 8 weeks. Secondary outcomes included $>$ 50% pain relief at 3 months, relatively good patient satisfaction, and adverse events.

Quality Assessment in Individual Studies

The Jadad scale was used to evaluate the methodological quality of each RCT included in this meta-analysis.[31] This scale consisted of three evaluation elements: randomization (0–2 points), blinding (0–2 points), and dropouts and withdrawals (0–1 points). One point would be allocated to each element if they were mentioned in the article, and another 1 point would be given if the methods of randomization and/or blinding were detailed and described appropriately. If methods of randomization and/or blinding were inappropriate, or dropouts and withdrawals had not been recorded, 1 point was deducted. The score of the Jadad scale varies from 0 to 5 points. An article with a Jadad score ≤ 2 was considered of low quality. If the Jadad score was ≥ 3, the study was deemed high quality.[32]

Statistical Analysis

Mean differences (MDs) with 95% confidence intervals (CIs) for continuous outcomes (pain scores within 8 weeks) and risk ratios (RRs) with 95% CIs for dichotomous outcomes ($>$ 50% pain relief at 3 months, relatively good patient satisfaction, and adverse events) were used to estimate the pooled effects. An I^2 value $>$ 50% indicates significant heterogeneity. The random-effects model with DerSimonian and Laird weights was used in all analyses. Sensitivity analysis was performed to detect the influence of a single study on the overall estimate via omitting one study in turn when necessary. Owing to the limited number ($<$ 10) of included studies, publication bias was not assessed. A $p < 0.05$ in two-tailed tests was considered statistically significant. All statistical analyses were performed with Review Manager v.5.3 (The Cochrane Collaboration, Software Update, Oxford, United Kingdom).

Results

Literature Search, Study Characteristics, and Quality Assessment

The flowchart for the selection process and detailed identification is presented in ►**Fig. 1**. A total of 372 publications were identified through the initial search of databases. Ultimately, three RCTs were included in the meta-analysis.[25,27,28]

►**Table 1** summarizes the baseline characteristics of the three eligible RCTs in the meta-analysis. The three studies were published between 2016 and 2017, and sample sizes ranged from 40 to 46 with a total of 131. The PRP group and control group had similar characteristics at baseline. Two RCTs reported an intra-articular injection with PRP versus a steroid injection,[25,28] and one RCT reported intradiskal PRP versus a contrast agent.[27]

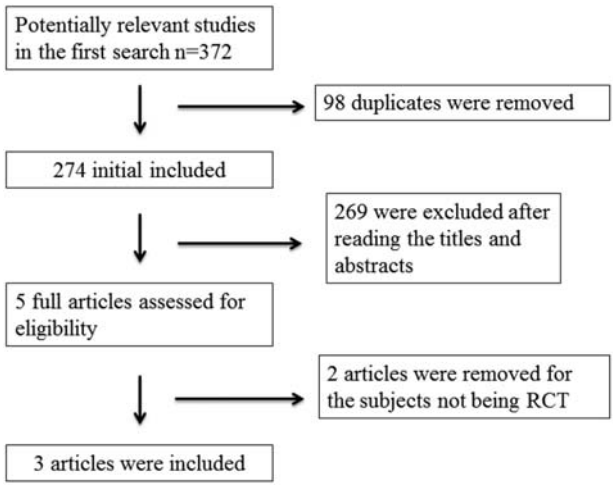

Fig. 1 Flow diagram of study searching and selection process. RCT, randomized controlled trial.

Table 1 Characteristics of included studies

No.	Study	PRP group					Control group						Jada scores
		N	Age, y	Male, *n*	BMI, kg/m^2	Methods	*N*	Age, y	Male, *n*	BMI, kg/m^2	Methods	Type	
1	Wu et al[28]	23	52.91 ± 7.60	10	22.56 ± 1.39	Intra-articular injection with PRP	23	52.78 ± 7.25	9	22.38 ± 1.45	Intra-articular injection with local anesthetic/ corticosteroid	Lumbar facet joint syndrome	5
2	Singla et al[25]	20	35.20 ± 12.86	16	23.69 ± 2.54	Ultrasound-guided sacroiliac joint injection with 3 mL leukocyte-free PRP with 0.5 mL calcium chloride	20	37.00 ± 10.89	16	22.41 ± 2.08	Ultrasound-guided sacroiliac joint injection with 1.5 mL methylprednisolone (40 mg/mL)	Sacroiliac joint pain	3
3	Tuakli-Wosornu et al[27]	29	41.4 ± 8.08	15	–	Intradiskal PRP	16	43.80 ± 8.91	9	–	Intradiskal contrast agent	Symptomatic degenerative intervertebral disk	4

Abbreviations: BMI, body mass index; PRP, platelet-rich plasma.

Among the three RCTs, two studies reported the pain scores within 8 weeks,[25,27] two studies reported > 50% pain relief at 3 months,[25,28] two studies reported relatively good patient satisfaction,[27,28] and three studies reported adverse events.[25,27,28] Jadad scores of the three included studies varied from 3 to 5; all three studies were considered high quality according to our assessment.

Primary Outcome: Pain Scores within 8 Weeks

These outcome data were analyzed with a random-effects model. The pooled estimate of the two included RCTs suggested that compared with the control group for low back pain, PRP injection was associated with significantly decreased pain scores (MD: – 1.47; 95% CI, – 2.12 to – 0.81; $p < 0.0001$), with no heterogeneity among the studies (I^2: 0%; heterogeneity $p = 0.84$) (►**Fig. 2**).

Sensitivity Analysis

No heterogeneity was observed among the included studies for the pain scores. Thus we did not perform a sensitivity analysis by omitting one study in turn to detect the source of heterogeneity.

Secondary Outcomes

Compared with control intervention for low back pain, PRP injection could substantially improve the number of patients with > 50% pain relief at 3 months (RR: 4.14; 95% CI, 2.22–7.74; $p < 0.00001$; ►**Fig. 3**) and offer relatively good patient satisfaction (RR: 1.91; 95% CI, 1.04–3.53; $p = 0.04$; ►**Fig. 4**) with no increase in adverse events (RR: 1.92; 95% CI, 0.94–3.91; $p = 0.07$; ►**Fig. 5**).

Discussion

PRP is an autologous blood derivative containing high concentrations of activated growth factors and cytokines (e.g., platelet-derived growth factor, transforming growth factor, fibroblast growth factor, insulinlike growth factor 1, and epidermal growth factor).[33–36] These elements serve as important humoral mediators to induce an anti-inflammatory effect and natural healing cascade by promoting cell proliferation, migration and differentiation, protein transcription, extracellular matrix regeneration, angiogenesis, and collagen synthesis.[37–39]

Our meta-analysis concluded that PRP injection resulted in significantly improved pain relief (as evidenced by the meta-analysis of pain scores within 8 weeks and > 50% pain relief at 3 months) and patient satisfaction for patients with low back pain. In addition, one included RCT revealed that PRP injection was able to result in sustained and more reduction in pain visual analog scores and lumbar functional improvements at the end of 6 months than local anesthetic using a corticosteroid. These results indicated autologous PRP served as the superior treatment option for longer duration efficacy for low back pain compared with corticosteroids. Patients with osteoarthritis of the hip, knee, and ankle experienced significantly favorable pain relief and functional improvement after intra-articular PRP injection.[40–42] A previous study

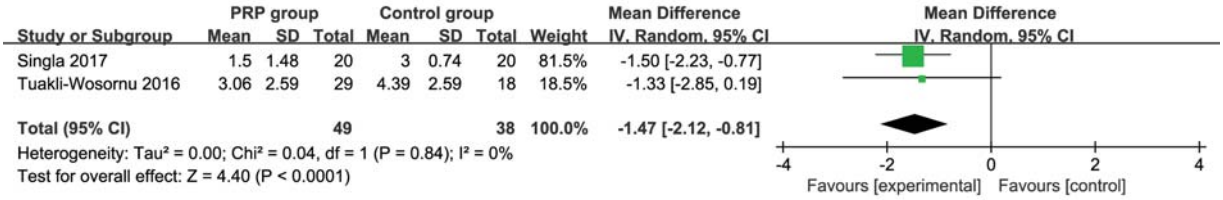

Fig. 2 Forest plot for the meta-analysis of pain scores within 8 weeks. PRP, platelet-rich plasma.

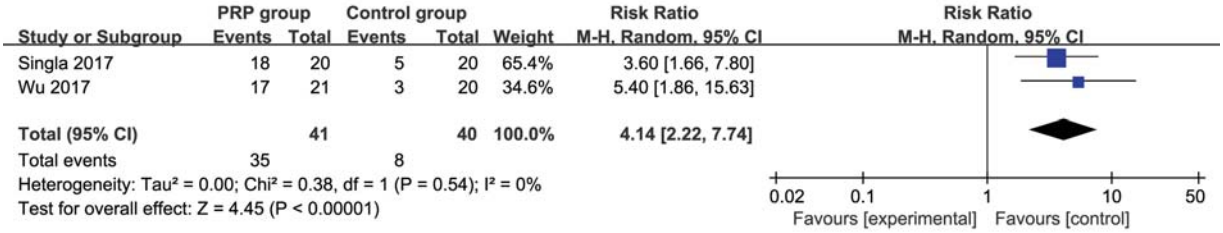

Fig. 3 Forest plot for the meta-analysis of pain relief at 3 months. PRP, platelet-rich plasma.

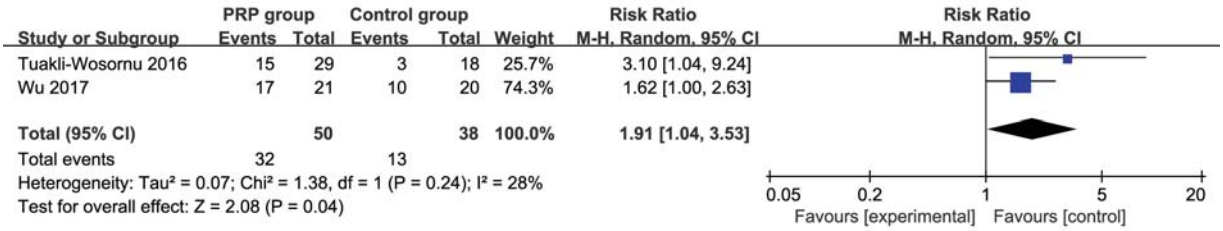

Fig. 4 Forest plot for the meta-analysis of relatively good patient satisfaction. PRP, platelet-rich plasma.

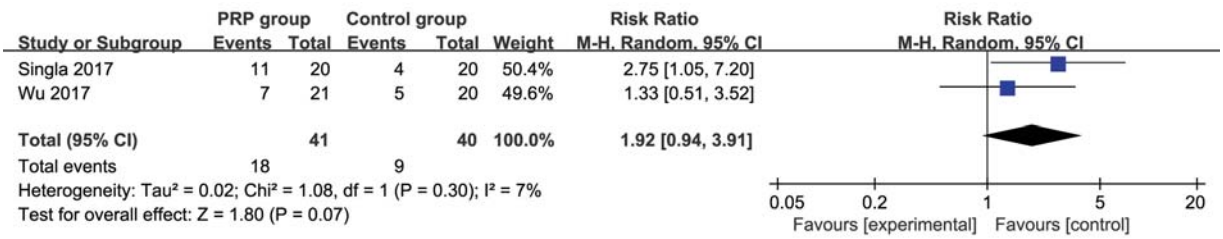

Fig. 5 Forest plot for the meta-analysis of adverse events. PRP, platelet-rich plasma.

demonstrated PRP injection produced better clinical outcomes than hyaluronic acid injection at 3 to 12 months posttreatment for knee osteoarthritis.[40]

The complications of PRP injection mainly included complications related to puncture and complications related to various drugs, but they all are exceedingly rare. The adverse events for PRP injection involved postinjection pain and stiffness, chest pain, and difficulty breathing, giddiness, and contralateral pain.[28] Our meta-analysis demonstrated no increase in adverse events after PRP injection compared with control group. All included RCTs reported no serious adverse events.

Several limitations should be considered. First, our analysis was based on only three RCTs, and all of them had a relatively small sample size ($n < 100$). Overestimation of the treatment effect was more likely in smaller trials compared with larger samples. The causes of low back pain in the included studies were different, and it may have had an influence on the pooling results. Next, the follow-up time of PRP varied from 3 months to 1 year, and longer durations were needed to confirm this issue. Finally, some unpublished and missing data might have lend bias to the pooled effect.

Conclusion

PRP injection showed an important ability to provide pain relief and patient satisfaction for those with low back pain. PRP injection is recommended to be administrated for low back pain with caution.

Conflict of Interest

None declared.

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