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Human Kinetics
CRITICALLY APPRAISED TOPIC

Platelet-Rich Plasma Compared With Other Common Injection Therapies in the Treatment of Chronic Lateral Epicondylitis

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Clinical Scenario: Lateral epicondylitis (LE) is a relatively common pathology capable of producing chronic debilitation in a variety of patients. A newer treatment for orthopedic conditions is platelet-rich plasma (PrP) local injection. ***Focused Clinical Question:*** Is PrP a more appropriate injection therapy for LE than other common injections such as corticosteroid or whole blood? ***Summary of Key Findings:*** Four studies were included: 1 randomized controlled trial (RCT), 2 double-blind RCTs, and 1 cohort study. Two studies involved comparisons of PrP injection to corticosteroid injection. One of the studies involved a 2-y follow-up while another involved a 1-y follow-up. Another study involved the comparison of PrP injection with whole-blood injection with a 6-mo follow-up. The final study included a PrP-injection group and control group. The 2 studies involving PrP vs corticosteroid injections with 2-y and 1-y follow-ups both favored PrP over corticosteroid injection in terms of pain reduction and function increases. The third study favored PrP injections over whole-blood injections at 6 mo regarding pain reduction. All studies demonstrated significant improvements with PrP over comparison injections or no injection. ***Clinical Bottom Line:*** PrP injections provide more favorable pain and function outcomes than whole blood and corticosteroid injections for 1–2 y after injection. ***Strength of Recommendation:*** Consistent findings from RCTs suggest level 1b evidence in support of PrP injection as a treatment for LE.

Keywords: elbow, orthopedics, orthopaedics, nonathlete

Clinical Scenario

Lateral epicondylitis (LE) is a condition that affects 1% to 3% of the population.[1] Research has shown that the physiology of LE involves microscopic tears with growth of regenerative tissue within the origin of the extensor carpi radialis brevis.[2] While the majority of individuals with LE do resolve their symptoms,[3] those who do not can experience chronic disease.[4] LE can result in lost playing time for athletes or perhaps even prematurely end a career. However, there is a growing body of evidence supporting platelet-rich plasma (PrP) injection for treatment of tendinopathy.

Focused Clinical Question

Is PrP a more appropriate injection therapy for LE than other common injections such as corticosteroid or whole blood?

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Summary of Search, "Best Evidence" Appraised, and Key Findings

- The literature search was conducted to limit studies with level 2 evidence or higher that investigated the effectiveness of PrP in the treatment of LE compared with corticosteroid, whole blood, or control group with no injection. Among the majority of studies,[4–7] participant compliance was satisfactory. However, 1 study[8] was unable to track compliance due to a multicenter approach.
- Five studies were included: 2 randomized controlled trials (RCTs), 2 double-blinded RCTs, and 1 cohort study.
- Two studies involved comparisons of PrP injections with corticosteroid injections.[5,6] One study[5] involved a 2-year follow-up while another[6] involved a 1- year follow-up. Another study involved the comparison of PrP injection with whole-blood injection with a 6-month follow-up.[4] Two studies included a PrP-injection group and control group.[7,8]
- The 2 studies[5,6] involving PrP versus corticosteroid injections both favored PrP over corticosteroid injection

due to increased pain reduction and function outcomes. The third study favored PrP injections over whole-blood injections at 6 months regarding pain reduction,[4] and the other 2 studies demonstrated favorable outcomes with the use of PrP injection compared with a control group.[7,8]

Clinical Bottom Line

There is strong evidence to support PrP injections as more effective in reducing pain in patients with LE when compared with alternative or no injection therapy.

Strength of Recommendation: There is level 2 evidence in support of PrP in reducing pain rather than whole-blood or corticosteroid injections in patients who present with LE. Although the studies presented were RCTs, 1 of them did present relatively low external validity.

Search Strategy

Terms Used to Guide Search Strategy

- **P**atient/Client group: *patients presenting with lateral epicondylitis*
- **I**ntervention: *platelet-rich plasma injection*
- **C**omparison: *injection, corticosteroid, autologous blood*
- **O**utcomes: *pain* and *function*

Sources of Evidence Searched

- PubMed
- MEDLINE (Ebsco)
- Literature cross-referenced for further resources

Inclusion and Exclusion Criteria

Inclusion

- Patients with lateral epicondylitis
- Treated with PrP, corticosteroid, or whole-blood injections
- Minimum 6-month follow-up
- Human subjects
- Articles in English published during or after 2005
- Minimum level 2 evidence

Exclusion

- Included patients without lateral epicondylitis
- Not available in English
- Follow-up less than 6 months
- Journals published before 2005
- Level of evidence below 2

Results of Search

Five relevant studies[4–8] were found and are presented in Table 1. However, only 4 studies are presented in Table 2 because 2 of the studies contained the same subjects but 1 contained a 1-year follow up[6] and the other a 2-year follow-up.[5]

Best Evidence

The studies included were identified as the best match in accordance with inclusion and exclusion criteria and due to the patient-centered outcomes assessed. Selection of these studies best compared PrP and other injection treatments for LE.

Implications for Practice, Education, and Future Research

Corticosteroid injections present a high frequency of relapse and recurrence in patients presenting LE.[9] At 6 weeks after corticosteroid injection, success rates were 92%, but at 52 weeks the success rate dropped to 69%.[9] However, studies have found that PrP can stimulate tendon-healing processes, as opposed to decreasing inflammation.[4] Platelets have a strong role in homeostasis and the normal healing process through growth-factor secretion.[4] These growth factors function in transforming growth-factor beta, vascular endothelial growth factor, and epithelial-growth-factor-enhancing tissue regeneration.[10] PrP contains a higher concentration, a mean of 539% greater, of platelets than whole blood.[7] One study reported that 3.31 million platelets were injected into each patient.[7]

Few studies are currently available that include PrP injection as a focused treatment for LE. In the studies reviewed for this critically appraised topic, comparisons of PrP with whole-blood injections,[4] corticosteroid injections,[5,6] and bupivacaine[7,8] (control group) occurred. In the studies that described their injection protocol, the time

Table 1 Summary of Study Designs of Articles Retrieved

Level of evidence	Study design	Reference
1	Randomized controlled trial	Peerbooms et al[6]
1	Randomized controlled trial	Gosens et al[5]
1	Randomized controlled trial	Thanasas et al[4]
2	Cohort study	Mishra and Pavelko[7]
2	Randomized controlled trial	Mishra et al[8]

Table 2 Characteristics of Included Studies

Article	Thanasas et al[4]	Gosens et al[5]	Mishra and Pavelko[7]	Mishra et al[8]
Design	RCT	Double-blind RCT	Cohort study	Double-blind RCT
Participants	28 consecutive patients diagnosed with chronic LE. Symptoms were present for 3 or more mo before intervention. Participants were split into a whole-blood-injection group or PrP injection and evenly distributed with 14 in each group. Participants had not had any injection therapy before this study. Block randomization was used to establish groups.	100 consecutive patients with LE. 49 participants were assigned to the corticosteroid group and 51 to PrP. Participants were scheduled for injection therapy between May 2006 and January 2008. All participants had LE for longer than 6 mo and pain of at least 50 on a VAS scale of 0–100 mm. Participants were at least 18 with a mean age of 47 y. The majority of participants were women. The majority of affected sides was the right elbow. Participants were randomly assigned by a computer program.	20 participants were included in the study with 15 in the PrP injection group and 5 serving as controls. All participants had a VAS score of at least 60/100 for at least 3 mo. The mean duration of symptoms for the PrP group was 15.3 mo with a mean participant age of 48.1 y. The mean duration of symptoms for the control group was 11.8 mo with a mean participation age of 42.2 y.	225 participants were included in the study with 112 receiving PrP injections and 113 serving as controls. All participants had a VAS score of at least 50/100 mm for at least 3 mo. The mean patient age in the control group was 47.4 y and the PrP-injection group 48.4 y. 12 sites were used for this study.
Intervention investigated	1 group was treated with a single injection of whole blood, the other group with 1 injection of PrP. Both groups received their injections into the deep aspect of the origin of the wrist extensors. Injections were conducted with ultrasound guidance. No nonsteroidal anti-inflammatories or cortisone was prescribed during follow-up. Oral paracetamol and ice therapy were allowed. Both groups were instructed to refrain from heavy labor for 1 wk. Flexibility and eccentric-loading programs were implemented. Reevaluations were conducted at 6 wk, 3 mo, and 6 mo after injection.	1 group was treated with corticosteroid injections, the other with PrP injections. Both groups received injections into the area of most tenderness and into the common extensor tendon. After injection no arm movement occurred for 15 min and complete rest ensued for 24 h after. Acetaminophen was allowed but no nonsteroidal anti-inflammatories. Stretching and strengthening programs were implemented, and after 4 wk normal sporting or recreational activity was allowed.	2 injections were given for each participant of both groups into the area of most pain and into the common extensor or flexor tendon. After injection no arm movement occurred for 15 min and complete rest ensued for 24 h. Participants were given a stretching protocol to follow for 2 wk. 4 wk postinjection, participants were allowed to return to normal sporting or recreational activity.	2–3 mL of prepared PrP was injected into the extensor carpi radialis brevis tendon; the control group received 2–3 mL of bupivacaine. Patients reported pain with resisted wrist extension. Baseline pain of resisted wrist extension was then compared at 4, 8, 12, and 24 wk post-PrP injection.
Outcome measures	*Primary Outcome:* Liverpool elbow score to assess range of motion, daily activities, and ulnar nerve status. *Secondary Outcome:* VAS on a scale of 0–10 to measure pain.	*Primary Outcome:* DASH. *Secondary Outcome:* VAS. Both outcomes were measured before injection and 8 weeks, 12 weeks, 26 weeks, 52 weeks, and 104 weeks postinjection.	*Primary Outcome:* A modified Mayo elbow score. *Secondary Outcome:* VAS.	*Primary Outcome:* Tennis Elbow Questionnaire. *Secondary Outcome:* VAS with resisted wrist extension.

(continued)

Table 2 *(continued)*

Article	Thanasas et al[4]	Gosens et al[5]	Mishra and Pavelko[7]	Mishra et al[8]
Main findings	Pretreatment VAS scores were 6.0 for the whole-blood group and 6.1 for the PrP-injection group. The PrP-injection group displayed better improvements in VAS scores than the whole-blood group at every reevaluation but was only significant at 6 wk. At 6 wk postinjection the PrP group displayed a mean improvement of 3.8 in VAS scores with the whole-blood group displaying a mean improvement of 2.5. No significant differences were noted according to the Liverpool score.	6 patients were lost during follow-up. Baseline characteristics did not significantly differ between groups; however, the PrP group did have higher DASH scores than the corticosteroid group before treatment. VAS scores temporarily got worse for the corticosteroid group between 8 and 26 wk; however, the PrP group displayed consistent significant improvements. The PrP group displayed significantly worse VAS scores at 4 wk postinjection but displayed significantly better VAS scores at 26, 52, and 104 wk postinjection than the corticosteroid group. DASH scores presented similar trends as VAS scores with the PrP group displaying significantly better scores 26, 52, and 104 wk postinjection than the corticosteroid group.	At 4- and 8-wk follow-ups the PrP-injection group experienced significantly greater reductions in VAS scores and Mayo elbow scores than the control group. During the final follow-up the PrP group reported a 93% reduction in pain compared with baseline. 93% of PrP participants were completely satisfied with their treatment, displaying 10 or less on the 0–100 VAS. PrP participants reported a mean of engaging in 99% of activities of daily living and 94% of their work or sporting activities.	42 adverse events were reported postinjection, of which 20 occurred in the control group and 22 in the PrP-injection group. At the final 24-wk follow-up a success rate of 83.9% was found in the PrP-injection group and 68.3% in the control group. Pain scores improved by 82.1% in the PrP injection group and 60.1% in the control group at 24 wk. No significant difference was found between the PrP-injection group and control group at 4, 8, or 12 wk.
Level of evidence	1	1	2	2
Validity score	9/11 on PEDro Scale	10/11 on PEDro Scale	6/11 on PEDro Scale	11/11on PEDro Scale
Conclusion	PrP injection has been shown to decrease pain more quickly than whole-blood injections and may provide a better treatment protocol due to PrP-injection safety and reduction of cost.	A single injection of PrP was shown to improve function and decrease pain more than corticosteroid injections during a 2-y follow-up with no reported complications.	Buffered PrP injections may be an alternative to surgery in individuals who have severe elbow tendinosis and have had failed nonoperative treatment. PrP-treated individuals experienced significant long-term improvements with no reported complications.	PrP injections may provide an alternative to surgery in patients who have chronic tennis elbow lasting 3 mo or longer. Compared with a control group, statistically significant differences were noted at 24 wk follow-up.

Abbreviations: RCT, randomized controlled trial; LE, lateral epicondylitis; PrP, platelet-rich plasma; VAS, visual analog scale; DASH, Disabilities of the Arm, Shoulder, and Hand.

from withdrawal of the patient's blood to PrP injection was approximately 30 minutes.[6,7]

Four of the studies[4,6–8] injected 2 to 3 mL of PrP into each patient, and the study[4] that compared PrP with whole-blood injected 3 mL of whole blood. The study that compared PrP with a corticosteroid injected 1 mL into the patient.[6]

After the PrP injection, participants were instructed to rest for 15 minutes and limit use of their arm for the next 24 hours.[5–7] After 24 hours, participants were instructed on a stretching and strengthening program for 2 weeks; 4 weeks after the injection, patients could return to sporting or recreational activities.[5–7] In another study patients were reassessed after 1 week and instructed on stretches and eccentrically loaded exercises to be performed twice per day for 5 weeks.[4] However, 1 study[8] did not mention any at-home instruction given to the participants.

Two studies reported that some patients experienced pain and discomfort at the injection site that slowly subsided within the first week after injection.[4,8] The pain and discomfort reported occurred in 2 of 112 patients receiving PrP injections.[8] However, another study reported no complications at any period after the injection.[7] Thanasas et al[4] found that the PrP-injection group presented better VAS scores at 6 weeks, 3 months, and 6 months during follow-up. However, the difference was significantly better than with whole blood at 6 weeks and no other follow-up time point.[4] Other research,[8] when comparing PrP injections with a control group, found that the difference in improvement was only significant at 24-week follow-up and not any time sooner. Improvements of 46% in VAS scores and 42% in Mayo elbow scores were noted at 4 weeks in another study.[7] Later, at 8 weeks after injection, patients reported an improvement of 60% in VAS scores and a 52% improvement in Mayo elbow scores over baseline.[7] Six months after the injection an improvement of 81% in VAS scores and 72% in Mayo elbow scores over baseline was noted in the PrP-injection group.[7] At the final follow-up (mean 25.6 months, range 12–38) a 93% improvement in VAS over baseline was recorded, and 93% of the patients reported satisfaction with the PrP treatment.[7]

In 1 study, corticosteroid injections provided better short-term outcome, but PrP injections provided better long-term outcomes.[6] Four weeks after injection, PrP patients reported a 21% improvement in their VAS scores and the corticosteroid patients reported a 32.8% improvement. In addition, at 4 weeks, Disabilities of the Arm, Shoulder, and Hand (DASH) scores improved 15.7% in PrP patients and 25.8% in corticosteroid patients. Eight weeks after the injection, a 33.1% improvement of VAS scores was recorded for PrP patients and corticosteroid patients reported a 34.8% improvement. Recordings of VAS and DASH scores were also recorded at 12 weeks, 6 months, and 1 year (although this study continued in a later publication[5]). At 1 year the PrP patients reported a mean improvement of 63.9% in their VAS score, with the corticosteroid group reporting a 24% improvement. During a 2-year follow-up investigation, the PrP group recorded a DASH score of 17.6 ± 24 and a VAS score of 21.3 ± 28.1.[5] The corticosteroid group recorded a DASH score of 36.5 ± 23.8 and a VAS score of 42.4 ± 26.8. Recurrence rate and need for future treatment was higher in the corticosteroid group than in the PrP group.[5] A noteworthy finding is that the PrP group presented DASH scores that were worse before their injection than at their 26 week follow-up.[5] One study reported that PrP injections are twice as expensive as corticosteroid injections, but surgery is twice as expensive as PrP injections in cases of LE, although those findings were reported in Sweden.[5] Other reports[8] have shown that surgery can cost upward of $12,000 for chronic lateral epicondylar tendinopathy, while PrP injections cost as little as $1000.

Future research is needed to study the effects of PrP injections on LE in the athletic population. While the highlighted research articles provide favorable evidence on long-term outcomes when using PrP injections for LE, nonathletic populations were used. Therefore, evidence is lacking as to whether PrP injections provide favorable outcomes for those participating in competitive sports. More research is warranted regarding other orthopedic injuries and tendinopathies beyond LE.

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