Original Article

Functional Outcomes of Ultrasound-guided Platelet Rich Plasma Injection in Recalcitrant Lateral Epicondylitis After Steroid Injection: A Case Series

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Background: Platelet rich plasma [PRP] contains several growth factors which can improve functional outcomes in tendinopathies, especially tennis elbow. However, there have been no reports on the clinical use of PRP injection in patients who have had previous corticosteroid injections.

Objective: PRP injection can improve elbow function in patients with elbow tendinopathy who have a history of previous corticosteroid injection.

Materials and Methods: Sixteen lateral epicondylitis (tennis elbow) patients who had recurrent symptoms or treatment failure with previous corticosteroid injection therapy were included in the present study. Autologous PRP was injected into the extensor carpi radialis brevis [ECRB] origin of each patient to the ECRB under ultrasound guidance to improve the accuracy of the injection. Follow-up time, Visual Analog Scale [VAS] score, Disabilities of the Arm, Shoulder and Hand [Quick DASH] score, Mayo elbow score, and patient's satisfaction score were comprehensively collected both before and after PRP injection to evaluate functional outcomes.

Results: Three patients were lost to follow-up; 13 patients were analyzed in this case series. Mean follow-up time was 16.94 months. VAS score, Quick DASH score, and Mayo elbow score were significantly improved after treatment (8.78 versus 1.78, 47.35 versus 5.48, and 65.42 versus 96.25 respectively, $p<0.0001$). All patients were satisfied with treatment as demonstrated by the patient satisfaction scores. There were no complications from skin allergies after PRP injection. Interestingly, no patients had undergone surgery as of the last follow-up.

Conclusion: Ultrasound-guided PRP injection can improve functional outcomes in lateral epicondylitis patients who have had prior corticosteroid injections.

Keywords: Platelet rich plasma, Recalcitrant lateral epicondylitis, Recurrent lateral epicondylitis, Corticosteroid, Ultrasound-guided injection

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Lateral epicondylitis or tennis elbow is a common cause of lateral side elbow pain in orthopedic outpatients. Abnormal use of the elbow and extensor tendon[1] can result in repetitive micro-injury[2] and can lead to avascular necrosis and degenerative change of the common extensor tendon[3]. The tendon pathology primarily stimulates elbow pain and limits the functional activities of the patient[4,5]. Current treatments of this condition include physiotherapy, injection therapy[1], and surgical ECRB tendinosis resection.

Recently, the use of cellular based injection therapy for Tennis Elbow has been reported. Several

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studies have suggested that platelet rich plasma injection [PRP] was more effective and safer than corticosteroid injection in both short term and long term clinical outcomes[1,3-9]. According to the histological findings of tendon pathology, this condition has been shown to involve avascular necrosis and degenerative tissue and to not be inflammation or tendinitis[2]. PRP, which contains numerous growth factors [GFs], can stimulate the tissue regeneration process more precisely than corticosteroids [CS] whose function is to inhibit inflammation[1-3,10-12]. Most prior studies of PRP treatment recruited patients who had never received a CS injection. However, there are no reports which directly describe the results of PRP injection in patients who have had a previous CS injection.

Conservative treatment, e.g., activity modification, eccentric loading exercise, NSAID, and a tennis elbow strap, has been generally recommended as the first line of management[1,10,13,14] for lateral epicondylitis. Some patients who did not responded to these conservative measures received a CS injection because of its availability and cost saving. A number of patients still had recalcitrant symptoms after the CS injection[6]. In those cases, surgery may be required.

PRP has an additional benefit over CS[15] in that it is a potential option before considering surgery for patients who have failed to respond to CS injection. However, there only limited evidence regarding the functional results of PRP treatment in tennis elbow patients who have failed to respond to CS injection. In this case series, we evaluated the functional outcomes of PRP injection in cases of recurrent but unsuccessful treatment with corticosteroid injection. We also reviewed the relevant literature on platelet rich plasma and corticosteroid injection in lateral epicondylitis.

Materials and Methods

After receiving approval from the Ramathibodi Hospital Ethical Committee, the study was conducted in the outpatient clinic of Ramathibodi Hospital between January 2014 and January 2016. Initially, we included 16 consecutive cases of lateral epicondylitis who had a previous history of treatment failure with corticosteroid injection at the affected site. The clinical diagnosis criteria were recalcitrant lateral epicondylitis revealed by failure of corticosteroid treatment and suffering from lateral side elbow pain for more than 6 months[16]. Physical examination showed tenderness on the lateral epicondyle and pain at the same point when performing resistance wrist extension and middle finger extension tests. All tests were conducted by an experienced hand surgeon. Patients with cervical radiculopathy, inflammatory arthritis, elbow skin lesion, osteoarthritis of the elbow, a history of elbow fracture, or previous elbow surgery were excluded from the study. Participating patients were provided the PRP procedure.

Technique of PRP preparation and injection

All patients were informed of the study and the procedure was described to them prior to giving their consent to participate. Ten ml of autologous blood was withdrawn from an antecubital vein of the patient. The platelet-rich plasma fraction was obtained using a single round centrifuge-based technique. A double syringe system was used and samples were placed in a centrifuge and concentrated for 5 minutes at 1,500 rpm. Then the supernatant, which was PRP, was transferred to a prepared syringe using sterile technique and the RBC and WBC components were discarded. Approximately 2 ml of PRP was obtained from each patient. Finally, all patients received an autologous platelet rich plasma injection at the point of maximum tenderness under ultrasound guidance. The needle was confirmed to be at the ECRB origin before injection to increase the accuracy. The procedure was performed within approximately 20 minutes in the orthopedic outpatient clinic by the same hand surgeon and certified nurse who did the blood management. This protocol is the universally accepted method for PRP preparation.

Post-treatment protocol

The patients were asked to remain in a supine position for 10 minutes with a cold compress for pain relief. NSAID was prohibited, but acetaminophen was allowed for pain management. After the one week follow-up, stretching exercises for the ECRB tendon were initiated as a home program. An eccentric loading exercise was permitted 3 weeks after the injection, and normal household activities were allowed when pain symptoms subsided. Baseline data were collected initially and mean follow-up time, Mayo elbow score, visual analog scale [VAS] score[1,6], and Quick DASH score were recorded both before PRP injection and during each follow-up visit and by telephone interviews. Patient satisfaction questionnaires[17] were evaluated at the time of the last follow-up (Table 1).

Statistical analysis

The paired t-test was used to compare data before PRP injection and at the last follow-up for all patients. The *p*-values <0.05 were considered to be a

Table 1. Patient satisfaction questionnaires

Level of satisfaction after platelet rich plasma injection	Level of satisfaction after corticosteroid injection but before platelet rich plasma injection
1. Very pleased 2. Pleased 3. Not pleased 4. Very disappointed	1. No pain 2. Very much improved 3. Slightly improved 4. Same 5. Worse 6. Much worse

Table 2. Patient demographic data

Characteristics	Values
Total patients	16
Lost to follow-up	3
Age (years)	50.56 (SD 9.605)
Female [n, (%)]	9 (56.25)
Dominant hand: right, left	16, 0
Affected elbow: right, left	10, 6
Duration of symptoms (months)	14.88 (SD 10.80)
Previous steroid injections (n)	1.9 (range 1 to 4)
Joint comorbidity	0

statistically significant.

Results

Of a total of 16 patients, 3 were lost to follow-up and 13 patients were included in the final analysis. (Figure 1), The average age of the patients was 50.56 years (SD 9.6), the mean duration of symptoms was 14.88 months (SD 10.8), the mean number of previous CS injections was 1.9, and mean follow-up time was 16.94 months (SD 4.057). All the patients were right hand dominant. There were 10 affected right elbows. No joint comorbidity was present in any of the patients (Table 2).

There was a significant improvement at follow-up in VAS score, Quick DASH score, Mayo elbow score, and patient satisfaction compared to pre-injection (Table 3 to 5). Pre- and post-injection mean VAS scores were 8.78 and 1.78 (p<0.0001, SD 1.847, 1.626). Pre- and post-injection mean Quick DASH scores were 47.3 (SD 14.86) and 5.48 (SD 6.45) (p<0.0001), respectively. Pre- and post-injection mean Mayo elbow scores were 65.42 (SD 9.87) and 96.25 (SD 6.78) (p<0.0001), respectively. For the patient satisfaction score, the average level of satisfaction post-injection was 1.38 and the average satisfaction score before treatment was 1.46. There were no complications from skin allergies after PRP injection. None of the patients underwent an operation on the affected arm.

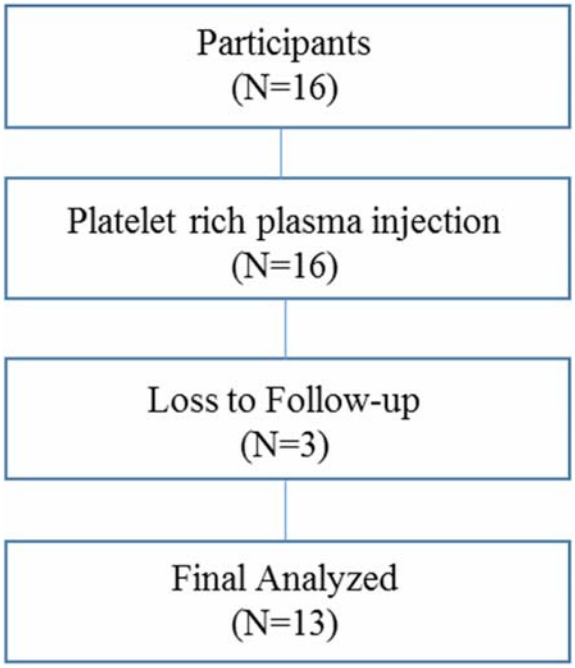

Figure 1. Flow diagram of platelet rich plasma injection for recalcitrant lateral epicondylitis study.

Discussion and Literature review

The aim of this case series study was to report the clinical outcomes of patients recalcitrant to corticosteroid who received a PRP injection. The study demonstrated the efficacy of the PRP injection in treatment of recalcitrant lateral epicondylitis as evidenced by improvement in VAS score, Quick DASH score, Mayo elbow score, and patient satisfaction after

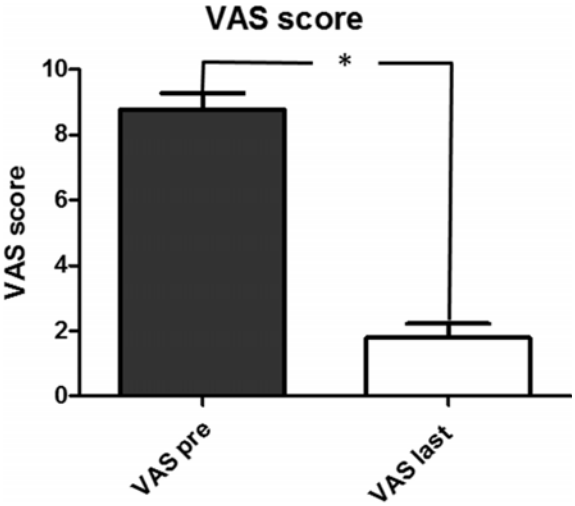

Figure 2. Visual analog score (VAS) comparing before injection and at last follow-up (*p<0.0001).

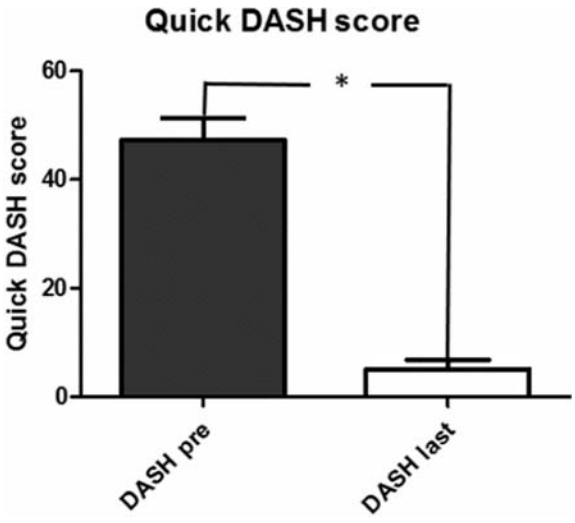

Figure 3. Quick DASH score comparing befored injection and at last follow-up (*p<0.0001).

the injection which reflects elbow functional outcomes from PRP therapy. None of the cases had required surgery as of the 16 month follow-up.

Platelet rich plasma is presently available and has become more popular in orthopedic society, rehabilitation and rheumatology units, especially for chronic tendinopathy such as lateral epicondylitis, Achilles tendinopathy, plantar fasciitis, and patella tendinopathy[5,9]. Several studies have reported better patient functional results with PRP injection

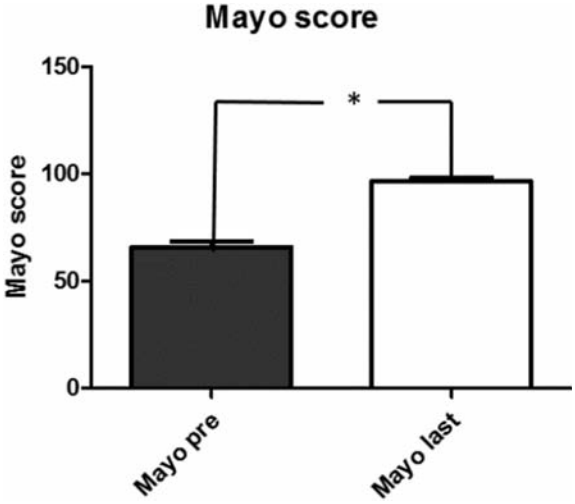

Figure 4. Mayo elbow score comparing before injection and at last follow-up (*p<0.0001).

therapy for lateral epicondylitis compared to other substances[1,3,6,8,11,12,15,18]. Arirachakaran et al in a systemic review and network meta-analysis reported that PRP injections significantly improved VAS and DASH scores compared to CS. Patients with PRP treatment had better VAS scores compared to those who received autologous blood [AB] injection treatment[1]. In terms of adverse effects, AB injection has a higher risk of complications than PRP injection because AB contains leukocytes which are antigen-presenting inflammatory cells[19]. It has been suggested that because PRP can reduce pain and has fewer complications than other injection therapies, it should be a preferred option for lateral epicondylitis. This treatment provides promising results with minimal risk of tendon degradation.

A recent report on steroid injection for tennis elbow by Kahlenberg et al investigated the histopathology of resected tissue and found that steroids may be harmful to the tendinopathy process and delay healing of the tendon[2]. This result is supported by a systematic review and network meta-analysis by Dong et al which notes that steroids are not recommended for use in the lateral epicondylitis because the data suggest it is a suboptimal choice compared to other substances[10]. Furthermore, steroid injection has been reported to have a high rate of symptom recurrence and treatment failure[8]. The efficacy of this non-biological substance seems to not only provide sub-optimal short term clinical outcomes, but also shows inferior long term efficacy compared to

biological substances such as PRP.

A number of recent studies of lateral epicondylitis injection include efficacy comparisons among substances, including PRP vs. CS, and AB vs. PRP in lateral epicondylitis in a population of patients who were naive to treatment. In common practice, however, many patients have previously received a CS injection. However, none of the studies have directly reviewed the results of treatment in patients who have had prior CS treatment of lateral epicondylitis. This study demonstrates the results of PRP treatment in this particular condition, i.e., patients who have already had CS treatment. The ultrasound assisted technique was used for guidance in order to increase injection accuracy[20,21] compared to unguided or "blind" injection. The outcomes of this study showed clinically significant improvement in elbow function, pain relief, and patient satisfaction. The authors believe that the PRP fraction contains a high concentration of platelet-rich plasma containing essential components for orthopedic tissue engineering, e.g., platelet-derived growth factor [PDGF], insulin-like growth factor-1 [IGF-1], transforming growth factor-β [TGF-β], and fibroblast growth factor-2 [FGF-2], mediators that stimulate progenitor cell or mesenchymal stem cell [MSC] proliferation[22]. In addition, each of these biological substances also stimulate tissue healing in cases of tissue degeneration due to chronic diseases to regeneration of tissue damaged by tendinopathy. Pain was eliminated by this process and elbow function was finally restored. Based on the results of this study, the authors suggest that PRP can be an option even in patients with recurrent pain from CS injection. Patients should be informed about this treatment before considering the operative management.

Limitations

The limitations of the present study were the small sample size and that, as a case series, it lacked randomization. Further clinical randomized controlled studies should be conducted to compare the functional outcomes between PRP injection and ECRB release in patients with recalcitrant lateral epicondylitis who have previously have had corticosteroid injection.

Conclusion

Platelet rich plasma may be considered as a useful treatment strategy for patients with recurrent symptoms from lateral epicondylitis after corticosteroid injection. PRP is safe and effective and can alleviate the need for surgery in tennis elbow in patients who have had previous CS injections.

What is already known on this topic?

Platelet rich plasma treatment in lateral epicondylitis provides better functional outcomes in both the short and long term compared to corticosteroid injection.

What this study adds?

This study provides additional evidence that platelet-rich plasma injection can be a beneficial therapy in patients with recurrent lateral epicondylitis after corticosteroid injection. Ultrasound guided injection may increase the accuracy of the PRP injection.

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Potential conflicts of interest

The authors declares no conflicts of interest.

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