Platelet-Rich Plasma Injection in Tennis Elbow

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ABSTRACT

Background:
Lateral Epicondylitis, often referred to as Tennis Elbow clinically.
Objectives:
This study aimed to evaluate the functional outcome after Platelet-Rich Plasma injection in patients suffering from lateral epicondylitis (Tennis elbow).
Patients and methods:
A prospective study was performed at the Orthopedic Surgery Department, Menoufia University Hospitals, and Sheikh Zayed Specialized Hospital. The material of this study included 50 patients with lateral epicondylitis (Tennis Elbow) who were considered to have local injections of platelet-rich plasma. The results were assessed at the end of the follow-up clinically using the VAS scale (visual analog of pain) and Modified Mayo Elbow Performance Score.
Results:
The average age was 40 years, with the earliest patient being 25 years old and the oldest patient being 58 years old. There were 30 males and 20 females, indicating a male predominance. The dominant side was afflicted in 42 patients (30 on the right side and 12 on the left side), while only eight patients (2 on the left side) had tennis elbow. Every patient exhibits a unilateral affection pattern. 8±2.6 months was the average duration of symptoms before injection, with a range of 4 to 13 months.
Conclusion:
Discomfort relief was achieved in the majority of patients (76%) with chronic epicondylitis, particularly those who had been refractory to other conservative treatments, following a single injection of platelet-rich plasma at the site of the elbow discomfort.

Keywords:
Platelet-rich plasma, Tennis elbow, Tendinopathy.

INTRODUCTION

In the clinical setting, Lateral Epicondylitis is frequently referred to as Tennis Elbow (1) A complex underlying pathogenesis that is not well understood is present in this condition. However, it is distinguished by uncomplicated indications of localized pain over the lateral epicondyle that is exacerbated by resisted wrist extension (2).

Lateral epicondylitis, the most common form of myotendinosis, is the result of consistent overuse of the extensor muscles in the wrist. In the common extensor tendon, which is derived from the lateral epicondyle, it is more specifically observed (3,4). Initially, epicondylitis was diagnosed as an inflammatory process. However, in 1979, it was defined as the disorganization of normal collagen architecture by invading fibroblasts in conjunction with an embryonic vascular reparative process.

"angiofibroblastic hyperplasia" was the name given to this reaction (3,4) It results in functional impairment and discomfort during a variety of daily activities. (4,5)

Conservative therapy and surgical interventions are employed to address this condition (6). Physical therapy, splinting, injectable and topical medicines (such as corticosteroids and botulinum toxins), and oral non-steroidal anti-inflammatory agents have all been the subject of numerous efficacy assessments (6). The tendon's inherent poor healing properties, which are a result of poor vascularization, are not altered by these traditional therapies. Consequently, PRP was proposed as a novel treatment for chronic tendinitis (7, 8).

The efficacy of PRP in human subjects is still PRP's clinical applications are relatively recent, which is likely why it is debatable. In 1987, after M. Ferrari underwent open-heart surgery to avoid homologous blood transfusion, it was first advertised as a component of autologous transfusions (9).

The human baseline blood platelets count is approximately 200,000 per microliter (µl) (150.000-400.000). Therapeutic platelet-rich plasma (PRP) concentrates the platelets by roughly fivefold approximately 1.000.000 platelets/ µl. (10)

PRP is highly versatile in its clinical applications, including orthopedics, wound healing, cardiothoracic, plastic, and maxillofacial surgery. In the treatment of chronic unhealed tendon injuries, such as those affecting the elbow, patella, and Achilles, platelet-rich plasma (PRP) is being utilized more frequently. Mishra and Pavelko Platelets are reported to contain a profusion of cytokines and growth factors that can influence the regeneration of soft tissue, muscle injury, and wounds, as well as postoperative blood loss and infection [5].

Barret and Erredge Platelets reportedly secrete a plethora of bioactive proteins that entice macrophages, mesenchymal stem cells, and osteoblasts. Proteins like these help with both the process of removing dead or damaged tissue and the process of regenerating and healing damaged tissue. [10].

There is ongoing debate regarding the mechanism of action of PRP, which may involve the stimulation and enhancement of the body's natural healing process. In particular, the molecules present in PRP preparation can function as an adjuvant, particularly during the matrix proliferation and inflammation phases [11]. Because of its high platelet concentration and active cytokines and GFs, platelet-rich plasma (PRP) acts as a vehicle for medications by enhancing physiological mechanisms. After the first explosion, thrombocytes continue to produce growth factors (GFs) and cytokines in vivo for the rest of their lives [11]. (i) platelet-derived growth factor (PDGF), (ii) transforming growth factor-beta 1 (TGF-b1), (iii) vascular endothelial growth factor (VEGF), and (iv) epidermal growth factor is the most notable of these [12]. Following this, macrophages arrive and initiate the production of their cytokines and GFs, some of which are comparable to those produced by platelets, as a result of the stimulation of vascular ingrowth. A new and ongoing local tissue repair and regrowth is the result.

[12]. Since PRP contains a larger concentration of platelets than whole blood, it is more successful in treating chronic non-healing tendinopathies, such as tennis elbow, and facilitating the healing process [13,14].

PATIENTS AND METHODS

The material of this study included 50 patients with lateral epicondylitis (Tennis Elbow) who were considered to have local injections of platelet-rich plasma at Sheikh Zayed Specialized and Menoufia University hospitals between February 2016 to November 2019.

The patients were followed for 6 months post-injection. Patients were categorized into two groups according to the number of local injections:

Group A: Included 38 cases (76 %) who received a single injection of PRP.

Group B: Included 12 cases (24%) who received two injections of PRP.

Positive findings from two of the following clinical tests: Included in the study were Cozen, Mill, Gardner, and Maudsley. The minimum age to participate was 20 years, and the oldest participant was 60 years old. Duration of symptoms continued for more than six weeks, with pain severity with a minimum score of 5 (Visual Analogue Scaling (0-10), Patients had failed with one of conventional therapy programs (nonsteroidal medication, bracing, or corticosteroid injections). Not included were these patients: Being a pregnant woman, A history of low hemoglobin levels (<7.0 g/dl), low platelet counts (<15,000 /µL), or bleeding disorders, as well as any recent fever or infectious illness during the past six months, A personal or family history of cancer, whether blood-related or otherwise, All inflammatory bowel disease patients, History of any bony abnormalities at the afflicted elbow, Trauma to the extremities' periphery, including radial nerve damage, cervical radiculopathy, and the afflicted elbow's carpal tunnel syndrome, Use of systemic steroids within the last three weeks, prior injection of local steroids within the last six weeks, history of surgical treatment for tennis elbow, and therapy with anticoagulant and antiplatelet drugs fourteen days before to injection are all contraindications.

Diagnosis:

- History taking.
- Clinical examination.
- Special Tests (Assessment of pain provoked by resisted movement): Cozen's test, Middle finger test (Maudsley's test), Mill's test
- Complete Blood Count (CBC).

Methods of Evaluation:

All patients were evaluated post-injection upon the outcome measure for upper limb functions through the VAS scale (visual analog of pain) and Mayo Elbow Performance Score and re-evaluated post-injection at two weeks, four weeks, and final evaluation at six months

Methods of PRP preparation [15,16]

At first, 20cc of venous blood was withdrawn with an aseptic technique from the antecubital vein of the contralateral side and transferred to the centrifuge (Fig.1). Two ml of citrate phosphate dextrose (CPD) were added for anticoagulation. The sample was distributed in 4 sterile tubes and then subjected to two stages of centrifugation. Initially, the erythrocytes were separated by centrifuging at 1600 rpm for 15 minutes. The supernatant plasma containing platelets was transferred to sterile containers that were devoid of anticoagulants.

Platelets were concentrated by employing a higher speed (2800 rpm for 7 minutes) during the second stage of centrifugation. Plasma-rich plasma (PRP) comprises the lower one-third, while platelet-poor plasma (PPP) comprises the upper two-thirds. At the tube's base, platelet particles were generated. The sterile syringe was used to extract platelet-poor plasma, and the platelet granules were suspended in a minimal quantity of plasma (2-4 mL) by gently agitating the tube. PRP-containing leukocytes comprised the final product, which was 2 mL. (Fig.2)

Figure 1 Centrifuge and tubes used in the procedure.

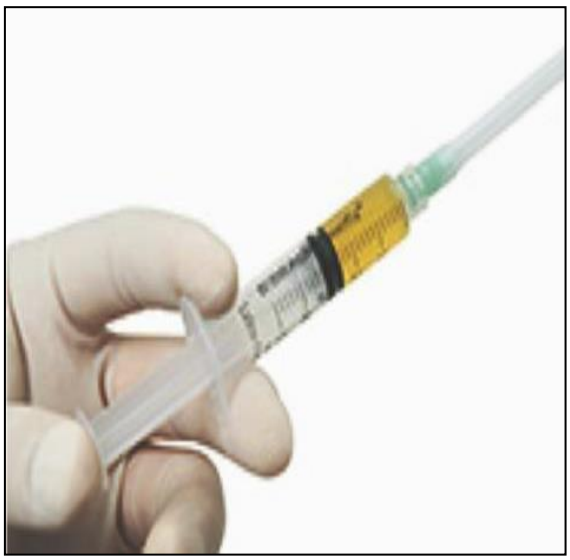

Figure 2 PRP final product.

PRP Activation

2% calcium chloride was added to the solution at a volume ratio of 7 to 1 to exogenously activate PRP before injection, thereby facilitating the release of growth factors [1, 17].

PRP Injection

The PRP was prepared and activated, and it was promptly used for local injection after being maintained in a sterile environment. With the afflicted arm rested at the side, the patient was supine with the elbow bent at 45 degrees and the wrist arched. Through careful palpation, the epicondyle's weakest spot is located and noted. A local anesthetic was provided (two milliliters of 1% lidocaine was injected eight minutes before the PRP injection) and the injection site was sterilized. Subsequently, two ml of liquid PRP were injected through a 22G needle in a sterile environment at the elbow's most tender point, using a peppering technique to spread the PRP in a clockwise fashion to achieve a more extensive delivery zone (Fig.3). Using this technique, a single cutaneous portal was used to inject platelet-rich plasma in identical volumes, with nine more tendon penetrations following.

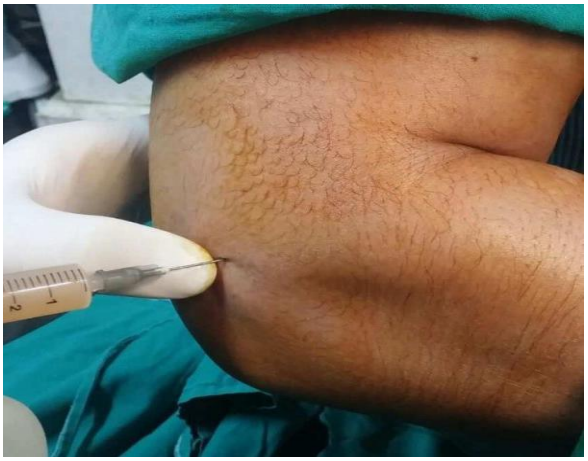

Figure 3 Technique of local injection of PRP in the elbow

Statistical analysis:

An IBM-compatible personal computer loaded with SPSS statistical software version 20 was employed to collect, tabulate, and statistically analyze the data.

Two types of statistics were done:

1) **Descriptive statistics:**
   - **A.** Qualitative data: number (No), percent (%).
   - **B.** Quantitative data: Mean(x-), standard deviation (SD), median, and range.
2) **Analytic statistics:**
   - **A.** Qualitative data: Chi-square test (X^2).
   - **B.** Quantitative data: Mann Whitney and student t-test.

P-value of greater than 0.05 was regarded as statistically insignificant. Statistically significant was defined as a P-value of ($\leq$0.05). Statistics were deemed highly significant when the P-value was less than 0.001.

RESULTS

Fifty patients undergoing treatment for chronic lateral epicondylitis with a local injection of platelet-rich plasma were prospectively studied for six months following injection. Based on the total number of local injections, patients were divided into two groups:

Group A: Included 38 cases (76 %) who received a single injection of PRP.

Group B: Included 12 cases (24%) who received two injections of PRP, those patients showed minimal improvement 4 weeks after first injection.

Group A: Patients showed a 42 % reduction of VAS Scale 4 weeks after injection, this progressed to 90% after 6 months of follow-up. Performing paired t-tests, there were significant differences between readings of pre-injection and final post-injection VAS Scale as p-value < 0.001.

Group B: Patients showed a 40 % reduction of VAS Scale 4 weeks after the second injection progressed to 87% after 6 months of follow-up. Readings of the pre-injection and final post-injection VAS Scale showed significant differences (p-value < 0.001) when a paired t-test was conducted.

Final End Results according to Mayo Elbow Performance Score in Both Groups:

Group A: The outcomes were favorable for all patients; 16 patients (42% of the total) had outstanding results and 22 patients (58% of the total) had good results.

Group B: Eight patients had satisfactory results (67%): 4 patients (33.3%) with excellent results and 4 patients (33.3%) with good results.

Four patients (33%) had unsatisfactory results patients (16.6%) a fair result and the other two (16.6%) with a poor result.

Total results in both groups after 6 months according to Mayo Elbow Performance Score are:

Satisfactory results were in 46 patients (92%) (20 patients (40%) with excellent results, 26 patients (52%) with good results). The unsatisfactory results were presented in four patients (8%) (two with a fair result (4%) and the other two with a poor result (4%))

Comparison between pre-injection & Final Mayo Elbow Performance Score after 6 Months in Both Groups.

Although group A had a higher mean pre-injection Mayo Elbow Performance Score (54.1) compared to group B (50.6), the difference was not deemed statistically significant (P value = 0.1857). Group A had a higher mean post-injection Mayo Elbow Performance Score (89.1) than Group B (82.5) after the follow-up period, however, the difference was not statistically significant (P value = 0.1413).

Satisfactory results in group A (100%) were higher than in group B (67%) the difference was found to be statistically insignificant (P value =0.7932).

The final results at the end of this study were Satisfactory results in 46 patients (92%) (20 patients (40%) with excellent results, and 26 patients (52%) with good results). The unsatisfactory results were presented in four patients (8%) (two with a fair result (4%) and the other two with a poor result (4%)). While every single patient in Group A had excellent results (16 out of 22), every single patient in Group B had satisfactory results (67%), two patients in Group B had fair results and two had poor ones. In group A, every single patient had excellent results, and every single patient in group B had good results.

DISCUSSION

Overuse injuries, such as tennis elbow, lateral epicondylitis, or repetitive strain injuries, affect the wrist extensor muscles. To be more precise, it is the most common type of myotendinosis that impacts the common extensor tendon and originates from the lateral epicondyle. [3,4]. Normal nonathletic populations are reported to have a prevalence of lateral epicondylitis ranging from 1 to 3% [5].

The 1979 classification of epicondylitis as "angiofibroblastic hyperplasia" changed the long-held belief that it was an inflammatory process. This new term describes the condition as the interference with normal collagen architecture brought about by invading fibroblasts and an underdeveloped vascular reparative response [3,4]. As a result, regular tasks become more difficult and painful [4,5]. Both conservative treatment and surgical interventions are part of the treatment options for this condition [5,6]. How well nonsteroidal anti-inflammatory drugs can be taken orally,

Several studies have looked at different medication options, such as topical and injectable options like botulinum toxins and corticosteroids, splinting, and physical therapy [5,6,7]. Traditional treatments do little to improve the tendon's poor vascularization, which makes its healing properties intrinsically poor [7,8]. New treatment options, such as prolotherapy, platelet-rich plasma (PRP), and autologous blood, aim to induce inflammation instead of suppressing it, taking into consideration the tendon's inherent characteristics [13,14]. PRP is a relatively new method of treating persistent tendinitis [6].

Autologous blood plasma fractions with platelet concentrations greater than baseline are known as platelet-rich plasma [8]. Platelets, which are present in both PRP and autologous blood, contain potent growth factors and granules that play an essential role in the recovery from long-term injuries [13,14]. Patients suffering from chronic nonhealing tendinopathies, such as tennis elbow, have reported better healing outcomes after receiving platelet-rich plasma (PRP) injections rather than whole blood

[6,13,14]. Platelet concentrations in therapeutic PRP should be four to six times higher than in whole blood (200000/mm3). At concentrations lower than or higher than this threshold, the healing process may be inhibited or rendered ineffective [6,14].

Patients suffering from persistently painful lateral epicondylitis were the subjects of this study, which aimed to track the results of injecting platelet-rich plasma locally. An injection of platelet-rich plasma was expected to hasten healing and alleviate pain, according to the study's hypothesis.

Several published studies have documented the use of local platelet-rich plasma or autologous blood injections to treat elbow epicondylitis. Several studies have shown that injecting patients with epicondylitis with platelet-rich plasma improves their symptoms. Heshtman et al (2011) [17] in a nonrandomized prospective study, Mishra and Pavelko (2006) [5] in a nonrandomized case series, and Peerbooms et al (2010) [6]. under the conditions of a controlled experiment with random assignment of participants. Differences in preparation, platelet activation method, and experimental design—for example, the length of time patients were unresponsive to conservative treatment—may contribute to the ongoing controversy surrounding the efficacy of local platelet-rich plasma injection.

Between February 2016 and November 2019, fifty patients with chronic lateral epicondylitis (tennis elbow) were included in the study. These patients were considered to have received a local injection of platelet-rich plasma. The average age was forty years, with the youngest being twenty-five and the oldest being sixty-eight. Forty patients reported symptoms on the dominant side (30 on the right and 10 on the left), while ten patients reported symptoms on the non-dominant side (10 on the left).

Participants in this study were divided into two groups: those who received one PRP injection (38 cases, or 76% of the total) and those who received two injections (24 cases, or 25% of the total) based on whether or not their symptoms improved significantly four weeks after the first injection. Everyone in this group worked in highly-demand occupations and had symptoms that lasted longer before the injection.

The reason why this group of patients' pain persisted after the first injection was because: (a) their pain was significantly worse before the injection (higher pre-injection VAS scale compared to those who had a single injection); (b) their symptoms persisted for a long time before the injection (nearly or more than a year); (c) they returned to their heavy-duty jobs at work very quickly; and (d) they all have labor-intensive, physically demanding jobs. In Hechtman et al (2011) [17], Raeissadat et al [18], and Gautam et al studies, all patients received only a single PRP injection.

In the Brkljac et al study (2015) [19] Every patient was administered a single PRP injection, with one of the three individuals who demonstrated a slight improvement in symptoms after the injection receiving a second one.

In Creaney et al [20] study, all patients received two PRP injections at 0 and 1 month to improve the outcome.

In this study, 50 patients underwent PRP injections locally; 38 patients received a single injection; all patients were followed up for 6 months; all had satisfactory results (16 patients with excellent results and 22 with good results); 12 patients received 2 injections; they continued to experience pain and were unable to return to work to their satisfaction one month after the first injection; after 6 months of follow-up, 8 patients had satisfactory results (4 patients with excellent results and 4 with good results); 4 patients had unsatisfactory results (2 patients with a fair result and the others two with poorly done). Thus, 46 out of 50 patients had satisfactory final results, while only 2 patients had unsatisfactory ones.

In group A, the mean VAS pain score dropped from 70 before injection to 7 at the end of the follow-up period.

From 54.1 before injection to 89.1 at the end of the follow-up period, that is the mean Mayo Elbow Performance Score. Group B's mean VAS pain score dropped from 73.7 before injection to 12 at the end of the follow-up period. Mayo Elbow Performance Score, which averaged 50.6 before injection, increased to 82.5 by the conclusion of the follow-up period.

Hechtman et al (2011) [17] One treatment of platelet-rich plasma injected using a peppering technique was administered to thirty-one patients (31 elbows) whose epicondylitis had not responded to nonsurgical treatment for more than six months, including steroid injection. Patients were monitored using a visual analog scale (VAS) for pain with five categories, which is a modified version of the American Shoulder and Elbow Surgeons assessment survey. One month after the injection, two patients (two elbows) opted to have surgery. With a success rate of 90% (28 out of 31 elbows), at follow-up visits, 28 out of 29 elbows reported a 25% reduction in pain. In the beginning, the average pain VAS score was 7.2±1.6 (n=30 elbows). After three months, it dropped to 4.0±2.2 (n=23), and at the final follow-up, it dropped to 1.1±1.7 (n=26). Using each patient as a control, we found a p-value of less than 01 when comparing baseline and follow-up scores.

Brkljac et al study (2015) [19] thirty-four patients, including eighteen women and sixteen men, all of whom had LE. We were able to successfully follow up with all patients for an average of 26 weeks, with a range of 6-114 weeks. Each patient claimed they

meticulously adhered to the post-operative protocols. Although thirty patients (86.2%) reported an improvement in their symptoms after receiving the injection, three patients (8.8%) reported the inverse phenomenon. Three more patients had a slight improvement in their symptoms after receiving the injection.

Raeissadat et al [18] Thirteen patients who received platelet-rich plasma (PRP) injections locally participated in the research. All outcomes, including VAS and Mayo scores, as well as PPT, were evaluated before the intervention. The outcome of the VAS evaluation the average VAS score did not change significantly (P 0.001) at any of the followup assessments or treatment-related 12-month assessments. There was a statistically significant improvement from the baseline score to all followup evaluations and the Mayo score twelve months after therapy (P 0.001). A 25% success rate was considered achieved when the VAS score decreased from baseline to all three follow-ups.

Gautam et al study [21] consisted of fifteen patients who underwent PRP injections locally. Evaluation tools used to evaluate patients included a visual analog scale (VAS) for pain, Disabilities of the Arm, Shoulder and Hand Scale (DASH) score, Oxford Elbow Score, modified Mayo Clinic performance index for the elbow (modified Mayo score), and all from pre-injection to the 6-month follow-up, there was a significant improvement. Creaney et al [20] Eighty patients who had not responded to conservative physical therapy were included in the study. A blinded investigator documented patient-related tennis elbow evaluations (PRTEEs) at baseline, 1, 3, and 6 months. The authors found that the PRP group had a 66% success rate and that 10% of patients ended up undergoing surgery after 6 months of follow-up.

Out of 50 patients enrolled in this study, 46 (38 in group A and 8 in group B) reported no pain in the epicondylar region afterward. Two individuals in group B continued to experience tenderness.

Thanasas et al [16] According to a 2011 study, nine out of fourteen participants in the platelet-rich plasma (PRP) group experienced injection-site localized pain and discomfort within the first seven days. Severe pain and tenderness were significantly reduced at the 6-month follow-up.

CONCLUSION

Patients with chronic epicondylitis, particularly those who had not responded to previous conservative treatments, reported significant pain relief after a single injection of platelet-rich plasma into the affected elbow (76%).

Certain groups of patients may show little improvement one month after the first injection making them unable to work satisfactorily, this group of patients are candidates for receiving a second local injection of PRP. Marked improvement was noticed in most of these patients (70%) after the second injection.

The outcomes were unaffected by the patients' ages, genders, hand dominance, or occupations.

Those whose symptoms persisted for a longer time before injection had less success with the first.

Injection required a second one, suggesting that this factor contributed to the overall outcome.

The benefits of platelet-rich plasma (PRP) therapy are debatable, but the risks are low. Although some participants reported increased pain at the injection site, this study did not record any instances of infection, tissue damage, or nerve injuries.

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