Platelet-Rich Plasma Injection in Tennis Elbow

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The Egyptian Orthopedic Journal; 2020 supplement (1), June, 55: 81-87

ABSTRACT

Background:
Lateral Epicondylitis, often referred to as Tennis Elbow clinically.
Objectives:
The aim of this study was 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 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 injection of platelets rich plasma. The results were assessed at the end of follow up clinically using VAS scale (visual analog of pain) and Modified Mayo Elbow Performance Score
Results:
The youngest patient was 25 years old, and the eldest patient was 58 years old with an average of 40 years. There were 30 males and 20 female showing male predominance. The dominant side was affected in 42 patient (30 right side and 12 left side) and only eight patient had tennis elbow in the non- dominant side (8 patients in the left side) All patients have unilateral affection pattern. The duration of symptoms before injection ranged from 4 to 13 months with a mean of (8±2.6) month. Satisfactory results were in 46 patients (92%) (20 patients (40%) with excellent results, 26 patients (52%) with good results). The un- satisfactory results presented in four patients (8%) (two with a fair result (4%) and the other two with a poor result (4%)).
Conclusion:
A single injection of platelet-rich plasma at the site of the elbow pain resulted in relief of pain in most of patients (76%) with chronic epicondylitis especially that had been refractory to other conservative treatments.
Key Words:
Platelet rich plasma, Tennis elbow, Tendinopathy

INTRODUCTION

Lateral Epicondylitis, often referred to as Tennis Elbow clinically[(1)] has complex underlying pathophysiology which is not well understood but is characterized by uncomplicated signs of localized pain over the lateral epicondyle which is made worse with resisted wrist extension[(2).]
Lateral Epicondylitis caused by repetitive overuse of the extensor muscles of the wrist is the most frequent type of myotendinosis occurring more specifically at the common extensor tendon that originates from the lateral epicondyle[(3,4).] Epicondylitis was initially believed to be an inflammatory process but in 1979, it was described as the disorganization of normal collagen architecture by invading fibroblasts in association with an immature vascular reparative response, which was termed "angiofibroblastic hyperplasia" [(3,4)] It causes pain and functional impairment in daily activities[(4,5)]
The treatment of this condition includes conservative therapy and surgical interventions[(6).] The effectiveness of oral nonsteroidal anti-inflammatory agents, topical and injectable medications including corticosteroids and botulinum toxins, splinting, physical therapy has been evaluated in many studies[(6)]. However, these traditional therapies do not alter the tendon's inherent poor healing properties secondary to poor vascularization so PRP was proposed as a new treatment used for chronic tendinitis[(7,8)].
Efficacy of PRP in human subjects are still debatable, probably because of the relatively recent clinical applications of PRP. First promoted by M. Ferrari in 1987 as an autologous transfusion component after an open-heart operation to avoid homologous blood transfusion[(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 five folds approximately 1.000.000 platelets/ µl. [10]

PRP has an extremely broad range of clinical applications in orthopedics, wound healing, cardiothoracic, plastic and maxillofacial surgery. PRP is increasingly used in treatment of chronic unhealed tendon injuries including the elbow, patella, and the achilles among others. Mishra and Pavelko Reported that platelets contain an abundance of growth factors and cytokines that can affect inflammation, postoperative blood loss, infection, osteogenesis and wound, muscle tear and soft tissue healing [5].

Barret and Erredge reported that platelets also release many bioactive proteins responsible for attracting macrophages, mesenchymal stem cells and osteoblasts that not only promote removal of degenerated and necrotic tissue, but also enhance tissue regeneration and healing [10].

The mechanism of action of PRP is still debated, and it may act by increasing and stimulating the natural healing process. The molecules contained in PRP preparation can act as adjuvant, especially in the phases of inflammation and proliferation of the matrix [11]. PRP acts as a drug delivery system since it comprises a high concentration of platelets and their active cytokines and GFs, which stimulate physiological processes. In vivo, following the initial burst, thrombocytes spend the rest of their lives synthesizing and secreting additional cytokines and Growth Factors (GFs) [11]. Of these, (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 are considered to be the most important [12]. Subsequently, through stimulation of vascular ingrowth, macrophages arrive and start producing their own cytokines and GFs, some are similar to those produced by platelets. This results in a new and continued local tissue repair and re-growth [12]. Due to higher concentration of platelets in PRP than whole blood, it was shown to have greater effect in the repair process in treatment of chronic non healing tendinopathies including tennis elbow [13,14].

PATIENTS AND METHODS

The material of this study included 50 patients with lateral epicondylitis (Tennis Elbow) who were considered to have local injection of platelets 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 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.

The inclusion criteria were a minimum age of 20 years and the oldest 60 years and positive findings from two of the following clinical tests: Cozen, Mill, Gardner and Maudsley. Duration of symptoms continued more than six weeks, with pain severity with minimum score of 5 (Visual Analogue Scaling (0-10), Patients had failure with one of conventional therapy programs (nonsteroidal medication, bracing, or corticosteroid injections). The following patients were excluded: Pregnant females, History of anemia (hemoglobin <7.0 g/dl), thrombocytopenia (platelets < 15,000 /µL) or history of bleeding dyscrasias, any recent febrile or infectious disease within 6 months, History of any malignancy (including hematologic and non-hematologic malignancies) ,Patients with rheumatoid arthritis, History of any bony malformations at the affected elbow, Peripheral nerve injury such as radial nerve injury, cervical radiculopathy, and carpal tunnel syndrome at the affected elbow, Treatment with anticoagulant and anti-platelet medications 14 days before injection, Previous use of systemic steroids within past 3 weeks ,Previous treatment with local steroid injection within 6 weeks, Previous surgical management of tennis elbow.

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 have been evaluated post-injection upon the outcome measure for upper limb functions through 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, 20 cc of venous blood were withdrawn with aseptic technique from 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 was subjected to two stages of centrifugation. The first stage of centrifugation was done at a speed of 1600 rpm for 15 minutes

for separation of erythrocytes. The supernatant plasma containing platelet was transferred into another sterile tubes (without anticoagulant). The second stage of centrifugation was done at a higher speed (2800 rpm for 7 minutes) in order to concentrate platelets. The lower 1/3rd is PRP and upper 2/3rd is platelet-poor plasma (PPP). At the bottom of the tube, platelet pellets were formed. Platelet Poor Plasma was removed using a sterile syringe and the platelet pellets were suspended in a minimum quantity of plasma (2-4 mL) by gently shaking the tube. The final product was 2 mL of PRP containing leukocytes (Fig.2)

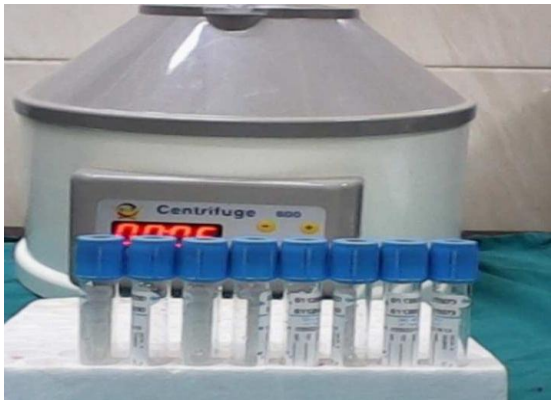

Figure 1: Centrifuge and tubes used in the procedure.

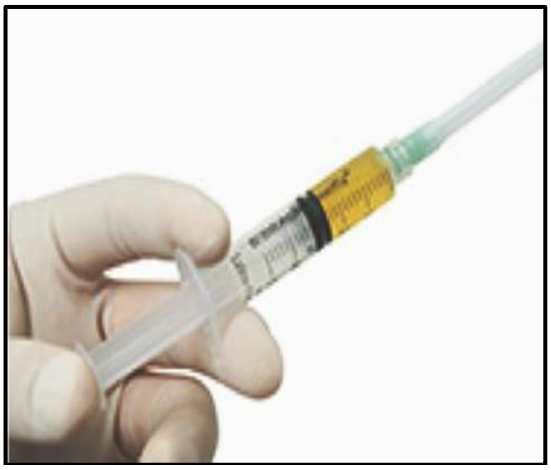

Figure 2: PRP final product.

PRP Activation

PRP activation prior to injection was done, exogenously by calcium chloride (the solution was mixed with 2% calcium chloride at a volume ratio of 7 to 1 to promote the release of growth factors) [1,17].

PRP Injection

Once the PRP was prepared and activated, it was maintained in a sterile environment and used immediately for local injection, the patient was placed in the supine position, the affected arm resting at the side with the elbow flexed to 45 degrees and the wrist pronated. The most tender point of the epicondyle is identified by gentle palpation then marked. Sterilization of skin at the site of injection was done and local anesthesia was applied (two mL of lidocaine 1% was injected 8 minutes before PRP injection) then two ml of liquid PRP were injected in a sterile condition using a 22G needle at maximal tender point at the elbow using a peppering technique spreading in a clock-like manner to achieve a more expansive zone of delivery (Fig.3). This technique involved a single skin portal followed by 9 multiple penetrations of the tendon while injecting equal amounts of platelet rich plasma.

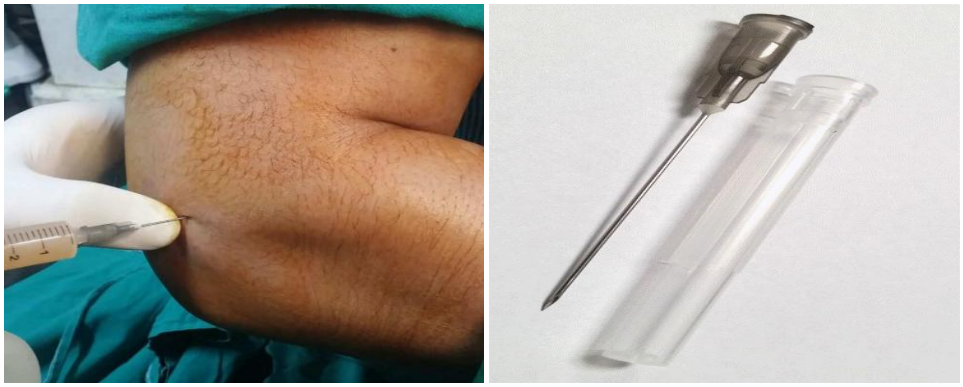

Figure 3: Technique of local injection of PRP in the elbow and 22G needle

Statistical analysis:

Data were collected, tabulated and statistically analyzed by an IBM compatible personal computer with SPSS statistical package version 20.

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 (>0.05) was considered statistically insignificant. P-value of (≤0.05) was considered statistically significant. P-value of (≤0.001) was considered statistically highly significant.

RESULTS

This prospective study was performed on 50 patients with chronic lateral epicondylitis treated with local injection of PRP and the period of follow up lasted for 6 months after injection.

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

Patients were categorized into two groups according to 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, those patients showed minimal improvement 4 weeks after first injection.

In group A, all patients had satisfactory results (16 patients with excellent results, 22 patients with good results), while in group B, 8 patients (67%) had satisfactory results (4 patients with excellent results, 4 patients with good results) and 4 patients (33%) were with un-satisfactory results (two patients with a fair result and the other two with a poor result).

Final End Results according to different methods of assessment:

I. Visual Analogue Scale of Pain:

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

Group B: Patients showed 40 % reduction of VAS Scale 4 weeks after the second injection progressed to 87 % after 6 months of follow up. Performing paired t-test, there were significant differences between readings of pre-injection and final post-injection VAS Scale as p-value < 0.001.

Comparison between pre-injection & Final VAS Scale after 6 Month in Both Groups

The mean pre-injection VAS Scale in group B (73.3) was higher than group A (70), the difference was found to be statistically insignificant (P value = 0.0543)

At the end of follow up period, the mean of post-injection VAS scale in Group B (10.1) was higher than group A (7), the difference was found to be statistically insignificant (P value = 0.0544).

II. Final End Results according to Mayo Elbow Performance Score in Both groups:

Group A: All patients had satisfactory results: 16 patients (42%) with excellent results and 22 patients (58%) with 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 un-satisfactory results:2 patients (16.6%) with a fair result and the other two (16.6%) with a poor result.

Total Final end 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 un-satisfactory results 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 Month in Both Groups:

The mean of pre-injection Mayo Elbow Performance Score in group A (54.1) was higher than group B (50.6), the difference was found to be statistically insignificant (P value = 0.1857).

The mean of post-injection Mayo Elbow Performance Score at the end of follow up period in group A (89.1) was higher than group B (82.5), the difference was found to be statistically insignificant (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 were in 46 patients (92%) (20 patients (40%) with excellent results, 26 patients (52%) with good results). The un- satisfactory results presented in four patients (8%) (two with a

fair result (4%) and the other two with a poor result (4%)). In group A, all patients had satisfactory results (16 patients with excellent results, 22 patients with good results), while in group B, 8 patients (67%) had satisfactory results (4 patients with excellent results, 4 patients with good results) and 4 patients (33%) were with un-satisfactory results (two patients with a fair result and the other two with a poor result)

DISCUSSION

Lateral epicondylitis known as tennis elbow is a repetitive strain injury caused by repetitive overuse of the extensor muscles of the wrist. It is the most frequent type of myotendinosis occurring more specifically at the common extensor tendon that originates from the lateral epicondyle[3,4]. The frequency of lateral epicondylitis is reported between 1 to 3% among normal nonathletic population[5].

Epicondylitis was initially believed to be an inflammatory process but in 1979, it was described as the disorganization of normal collagen architecture by invading fibroblasts in association with an immature vascular reparative response, which was termed "angiofibroblastic hyperplasia"[3,4]. It causes pain and functional impairment in daily activities[4,5]. The treatment of this condition includes conservative therapy and surgical interventions[5,6]. The effectiveness of oral nonsteroidal anti-inflammatory agents, topical and injectable medications including corticosteroids and botulinum toxins, splinting, physical therapy has been evaluated in many studies [5-7]. However, these traditional therapies do not alter the tendon's inherent poor healing properties secondary to poor vascularization[7,8]. Given the inherent nature of the tendon, new treatment options including platelets rich plasma (PRP), autologous blood, and prolotherapy are aimed at inducing inflammation rather than suppressing it[13,14]. PRP is quite a new treatment used for chronic tendinitis [6].

Platelet rich plasma is defined as a volume of the plasma fraction of autologous blood having a platelet concentration above baseline [8]. Both PRP and autologus blood contain platelets, and these platelets have strong growth factors and granules that have critical role in the healing process of chronic injuries[13,14]. Due to higher concentration of platelets in PRP than whole blood, it was shown to have a greater effect in the repair process in treatment of chronic nonhealing tendinopathies including tennis elbow[6,13,14]. Therapeutic PRP should have a platelet concentration 4 to 6 times greater than that of whole blood (200000/mm3). The concentrations less than or greater than this amount may be ineffective or inversely lead to suppression of the healing process[6,14].

The goal of this study was to follow the outcome of local platelet- rich plasma injection in patients with chronic painful lateral epicondylitis. The study hypothesis was that the platelet-rich plasma injection would stimulate the healing process manifested by a reduction in pain.

Several published studies have reported using local platelet-rich plasma or autologous blood injection to treat epicondylitis of the elbow. Positive results of platelet-rich plasma injection in patients with epicondylitis have been reported by 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]. In a randomized controlled trial. However, considerable controversy remains about the effectiveness of local platelet-rich plasma injection, which in part may be due to differences in preparation, method of platelet activation, and experimental design, such as how long patients were unresponsive to conservative treatment.

In this study 50 patients with chronic lateral epicondylitis (Tennis Elbow) were considered to have local injection of platelets rich plasma on the period from February 2016 to November 2019. The youngest was 25 years old, and the eldest was 58 years old with an average of (40 years). The dominant side was affected in 40 patients (30) right side and (10) left side) and only ten patients had tennis elbow in the non- dominant side (10 patients in the left side).

In this study patients 38 cases (76 %) received a single PRP injection and 12 cases (24%) received two PRP injections, those who showed minimal improvement in their symptoms 4 weeks after first injection so they received the second injection. All patients in this group they had longer duration of symptoms pre-injection and all of them had high demand occupations.

Persistence of pain in this group of patients after the first injection was due to the severity of the pain before the first injection with higher pre-injection VAS scale than those who received only single injection, the long duration of symptoms before injection (near or more than one year), early return of these patients to heavy activities in their work and also as they all have high demand occupations which require marked physical effort.

In Hechtman et al (2011) [17], Raeissadat et al [18], Gautam et al

studies, all patients received only single PRP injection.

In Brkljac et al study (2015) [19] all patients received single PRP injection and one of the three

patients who did show a very small improvement in symptoms following injection received a second injection.

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 received local injection of PRP, 38 patients received single PRP injection only, all patients were successfully followed up for 6 months, all had satisfactory results (16 patients with excellent results and 22 patients with good results), 12 patients receive 2 local injections as they showed minimal improvement one month after the 1st injection and still complaining from pain and they were unable to return to their work satisfactorily, after 6 months of follow up 8 patients of them ended with satisfactory results (4 patients with excellent results and 4 patients with good results), 4 patients ended with un-satisfactory results (2 patients with a fair result and the others two with a poor result). So, the final end results were satisfactory in 46 patients out of 50, only two patients had unsatisfactory results.

In group A, the mean of pre-injection visual analogue scale of pain was 70 and became 7 at the end of follow up period.

The mean of pre-injection Mayo Elbow Performance Score was 54.1 and became 89.1 at the end of follow up period.

In group B, the mean of pre-injection visual analogue scale of pain for this group was 73.7 and became 12 at the end of follow up period. The mean of pre- injection Mayo Elbow Performance Score was 50.6 and became 82.5 at the end of follow up period.

Hechtman et al (2011) [17] study included thirty-one patients (31 elbows) with epicondylitis unresponsive to nonsurgical treatment (including steroid injection) for >6 months received a single treatment of platelet-rich plasma injected with a peppering technique. Patients were followed using a 5-subcategory visual analog scale (VAS) for pain, modified American Shoulder and Elbow Surgeons assessment survey. Two patients (2 elbows) were elected for surgery 1-month post injection. Of the remaining 29 elbows followed, 28 had a 25% reduction of pain at follow-up visits, for an overall success rate of 90% (28 of 31 elbows). The mean for VAS scale of pain at baseline, 3 months, and last follow-up were 7.2±1.6 (n=30 elbows), 4.0±2.2 (n=23), and 1.1±1.7 (n=26), respectively (P<.01 or less comparing follow-up scores to baseline using each patient as his or her own control).

Brkljac et al study (2015) [19] included 34 (18 women and 16 men) patients who all suffered from LE. All patients were successfully followed up and the mean follow up time was 26 weeks (range 6–114 weeks). All patients had reported compliance with the post procedure protocol outlined. Thirty patients (88.2%) showed an improvement, three patients (8.8%) reported that their symptoms had progressed in severity following the injection. Another three patients who did show a very small improvement in symptoms following injection.

Raeissadat et al [18] study included 31 patient who received local injection of PRP, all outcomes including VAS and Mayo scores and PPT were measured before intervention. VAS score Mean VAS score decreased significantly at each follow up evaluations and at 12 months after therapy compared to baseline ($P < 0.001$). Post intervention Mayo score (12 months follow up) improved significantly in all follow up evaluations and at 12 months after therapy compared to baseline ($P < 0.001$). Success rate defined 25% as decrease in VAS score compared to baseline was achieved in all 3 follow ups).

Gautam et al study [21] included 15 patients who received local injection of PRP. Patients were assessed using the visual analogue 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), all improved significantly from pre-injection to the 6-month follow-up.

Creaney et al [20] study included 80 patients who had failed conservative physical therapy. Patient-related tennis elbow evaluation (PRTEE) was recorded by a blinded investigator at 0, 1, 3 and 6 months. After 6 months of follow up, the authors observed a 66% success rate in the PRP group & 10% of patients were converted to surgery.

In this study, Post-injection, there was no tenderness over epicondylar region in 46 patients out of 50 patients (38 patients in group A & 8 patients in group B). Tenderness persisted only in two patients from group B.

Thanasas et al [16] in 2011 reported that nine out of 14 in the PRP group, complained of local pain and discomfort at the injection site in the first week. At 6 months of follow up, significant reductions in pain and tenderness noticed.

CONCLUSION

A single injection of platelet-rich plasma at the site of the elbow pain resulted in relief of pain in most of patients (76%) with chronic epicondylitis especially that had been refractory to other conservative treatments

Certain group 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 age, gender, hand dominance and occupation of patients had no influence on the final results.

Duration of symptoms before injection had influence on the final end results, as those with longer duration of symptoms showed little improvement after the first injection and needed a second injection.

Even though the success of PRP therapy is still questionable, the risks associated with it are minimal. There may be increased pain at the injection site, but the incidence of other problems infection, tissue damage, nerve injuries were not recorded in the present study.

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