Functional outcome of ultrasound guided platelet rich plasma injection and corticosteroid injection for lateral epicondylitis

Dr. S Veera Kumar, Dr. M Antony Vimal Raj, Dr. Rajadurai M and Dr. Kathirazhagan S

DOI: https://doi.org/10.22271/ortho.2019.v5.i2i.64

Abstract
Platelet Rich Plasma (PRP) has created a huge significance in several medical grounds, including orthopaedics. Numerous studies have shown that Platelet Rich Plasma can be used in the management of bony as well as soft tissue injuries. Lately, Platelet Rich Plasma has been used for chronic enthesopathies like tennis elbow, plantar fasciitis, in sports medicine and also in cartilage regeneration. In this study we assessed and reported the efficacy of ultrasound guided autologous Platelet Rich Plasma and Corticosteroid injection

Keywords: Hip fracture; Bone turnover markers; CTX; PINP; Vitamin D

Introduction
Platelet Rich Plasma is a portion of blood with platelets concentrated in plasma. The functioning of platelet rich plasma is mainly governed by the growth factors in the alpha-granules. TGF-BETA 1, PDGF, VEGF, EGF are the growth factors seen in platelet granules. Their main role lies on the healing process of many tissues. Platelet derived growth factor (PDGF) has mitogenic activity for both osteoblast as well as mesenchymal cells. PGF also has mitogenic potential which will regulate collagen production. VEGF-vascular endothelial growth factor, TGF-β transforming growth factor beta, FGF-fibroblast growth factor, CTGF-connective tissue growth factor, IGF-insulin like growth factor have analogous properties. It is because of the above growth factors, that Platelet Rich Plasma is a suitable substance for differentiation and regeneration of tissues.

With increased biological healing capacity, Platelet Rich Plasma helps in the cure of tennis elbow and also the relapse rate will be low. In our study, we used Ultrasound Guided Intralesional injection of autologous Platelet Rich Plasma and Corticosteroid injection for the treatment of chronic tennis elbow.

Aims and objectives
To assess the efficacy of ultrasound guided autologous Platelet Rich Plasma and Corticosteroid injection.

Materials and methods
This is a prospective trial involving the patients in the Department of Orthopaedics, Government Kilpauk Medical College and Hospital from April 2017 to December 2018. Approval was obtained from Ethics Committee for Research in human beings before this study.
A total of 220 patients were included in this study. Out of this, 110 patients were injected with PRP and rest 110 patients were given corticosteroid injection. All the patients were selected based on the inclusion and exclusion criteria described. Patient were selected by random methods on lot basis.
All patients were treated as Out Patient. All the patients underwent same method of treatment.
All the patients were assessed based on the numerical pain scoring system which will be described. Among the study group 71% of Dominant hand involvement is found.

**Inclusion criteria**
1. Pain more than 3 months after failed conservative treatment
2. Patients should have pain score more than eight at the time of PRP and corticosteroid injection.
3. Patients should not had a local steroid injection in last 2 months.
4. Both male and female
5. Age- 18 years and above
6. Pain and tenderness over the lateral aspect of elbow

One of the test must be positive:
1. Cozen’s test

2. Mill’s maneuver
1. Cozen’s test: Ask the patient to make a firm fist. While the patient maintains this position, try to passively flex the wrist. Patient will feel pain at the lateral epicondylar region.

2. Mill’s maneuver: While the patient keeps his/her elbow firmly straight and wrist flexed, pronation of the forearm initiates pain at the lateral epicondylar region.

**Exclusion criteria**
- Less than 3 months duration
- Pain score less than eight
- Patients with diabetes mellitus
- Infection at the injection site
- Thrombocytopenia
- Patient on anti-platelet medications
- Pregnancy
- Patients younger than 18 years

**Informed consent**
After explaining the disease condition and treatment with PRP and Corticosteroid injection in their native language, informed consent was acquired from all the patients. All the patients agreed for the procedure and to participate in the study. The consent form was signed by all the patients and their nearest relative.

**Clinical diagnosis**
Diagnosis of tennis elbow was done when the patient experienced pain along the lateral aspect of the elbow joint. On dorsiflexion of wrist, this pain would worsen. On examination, localized tenderness was elicited over the lateral epicondyle of the patient.

**Preparation of PRP**
Platelet Rich Plasma was prepared using double spin centrifugation method. 15ml of patients own venous blood was withdrawn from antecubital vein under aseptic conditions and was collected in pre sterilized centrifuge four vacutainers vials. These centrifuge vials were preloaded with anticoagulant Acid Citrate Dextrose. This vacutainer was subjected to a first spin in a centrifuge at a speed of 2500 rpm for 10 minutes. After the first spin three layers appear.

**Technique of infiltration**
The most tender point was palpated under ultrasound guidance and the point is marked using a skin marker and the site was prepared for injection. Under aseptic condition, using a 21G and 1 1/2 inch needle, 1ml PRP is injected initially over the site with maximum tenderness and the needle is partially withdrawn and multiple punctures are made in the surrounding tissue (peppering technique). The surrounding tissue was injected with the remaining 1ml of platelet rich plasma.

**Follow Up**
Patients were followed up for 6 months. Follow up was done at second day after injection to find out any adverse reactions. All cases were protected with brace initially and given oral antibiotics for 1 weeks with cold fomentation, and then restoration with normal daily activities were allowed from the third week with stretching and physiotherapy. NSAIDS are contraindicated 1 week before and after the procedure. Opioid analgesics can be given. Follow-up was done at 1, 2, 4, 6 months. Patients were assessed subjectively using the numerical pain score.

**Results and analysis**
Patients were analyzed for pain relief subjectively at 1, 2, 4 and 6 months. The results are given below.

**Percentage reduction of pain**
Patients were analyzed for percentage reduction of pain. Percentage reduction of pain is obtained by calculating the percentage of the difference of pain score at every follow-up from initial pain score at the time of injection.

| Table 1: Percentage reduction of pain in PRP patients |
|-----------------------------------------------------|
| Gender    | Excellent | Good | Poor |
|-----------|-----------|------|------|
| Male      | 73%       | 20%  | 7%   |
| Female    | 82%       | 14%  | 4%   |

| Table 2: Percentage of pain reduction in corticosteroid group |
|--------------------------------------------------------------|
| Gender    | Excellent | Good | Poor |
|-----------|-----------|------|------|
| Male      | 36%       | 59%  | 5%   |
| Female    | 37%       | 55%  | 8%   |

| Table 3: First month recorded |
|-------------------------------|
| Group            | Frequency | Percent | Valid Percent |
|------------------|-----------|---------|---------------|
| PRP Valid        | 0% pain relief | 4       | 3.5       | 3.5       |
|                  | 1-49%     | 81      | 72.6      | 72.6      |
|                  | 50-99%    | 17      | 15.9      | 15.9      |
|                  | 100%      | 8       | 8.0       | 8.0       |
|                  | Total     | 110     | 100.0     | 100.0     |
| Corticosteroids  | 0% pain relief | 6       | 4.7       | 4.7       |
| Valid            | 1-49%     | 86      | 79.4      | 79.4      |
|                  | 50-99%    | 12      | 10.3      | 10.3      |
|                  | 100%      | 6       | 5.6       | 5.6       |
|                  | Total     | 110     | 100.0     | 100.0     |

| Table 4: First month recorded |
|-------------------------------|
| Group            | Frequency | Percent | Valid Percent |
|------------------|-----------|---------|---------------|
| PRP Valid        | 0% pain relief | 4       | 3.5       | 3.5       |
|                  | 50-99%    | 26      | 23.9      | 23.9      |
|                  | 100%      | 17      | 15.9      | 15.9      |
|                  | Total     | 110     | 100.0     | 100.0     |
| Corticosteroids  | 0% pain relief | 5       | 3.7       | 3.7       |
| Valid            | 1-49%     | 78      | 72.0      | 72.0      |
|                  | 50-99%    | 15      | 13.1      | 13.1      |
|                  | 100%      | 12      | 11.2      | 11.2      |
|                  | Total     | 110     | 100.0     | 100.0     |
Table 5: Fourth month recoded

| Group       | Frequency | Percent | Valid Percent |
|-------------|-----------|---------|---------------|
| PRP         | 0% pain relief | 4     | 3.5          | 3.5          |
|             | 1-49%      | 8       | 8.0          | 8.0          |
|             | 50-99%     | 80      | 71.7         | 71.7         |
|             | 100%       | 18      | 16.8         | 16.8         |
|             | Total      | 110     | 100.0        | 100.0        |
| Corticosteroids | 0% pain relief | 5     | 3.7          | 3.7          |
|             | 1-49%      | 40      | 36.4         | 36.4         |
|             | 50-99%     | 51      | 47.7         | 47.7         |
|             | 100%       | 14      | 12.1         | 12.1         |
|             | Total      | 110     | 100.0        | 100.0        |

Table 6: Sixth month recoded

| GROUP       | Frequency | Percent | Valid Percent |
|-------------|-----------|---------|---------------|
| PRP         | 0% pain relief | 4     | 3.5          | 3.5          |
|             | 1-49%      | 5       | 4.4          | 4.4          |
|             | 50-99%     | 84      | 76.1         | 76.1         |
|             | 100%       | 17      | 15.9         | 15.9         |
|             | Total      | 110     | 100.0        | 100.0        |
| Corticosteroids | 0% pain relief | 4     | 3.7          | 3.7          |
|             | 1-49%      | 28      | 25.2         | 25.2         |
|             | 50-99%     | 65      | 59.8         | 59.8         |
|             | 100%       | 13      | 11.2         | 11.2         |
|             | Total      | 110     | 100.0        | 100.0        |

Table 7: Distribution of side among study group

| Side       | Frequency |
|------------|-----------|
| Right side | 59%       |
| Left side  | 41%       |

Table 8: Percentage of total gender distribution

| Gender | Frequency |
|--------|-----------|
| Male   | 55%       |
| Female | 45%       |

Table 9: Group statistics

| Group       | N  | Mean | Std. Deviation | Std. Error mean |
|-------------|----|------|----------------|-----------------|
| PRP         | 110| 8.778 | 4.1693         | .03922          |
| Corticosteroids | 110| 8.8785 | .32824         | .21552          |
| PRP         | 110| 5.7965 | 2.37607        | .22352          |
| Corticosteroids | 110| 6.3084 | 2.22935        | .21552          |
| PRP         | 110| 4.2035 | 2.26053        | .21265          |
| Corticosteroids | 110| 4.9065 | 2.15675        | .20850          |
| PRP         | 110| 2.8673 | 1.80032        | .16936          |
| Corticosteroids | 110| 4.0561 | 1.93201        | .18677          |
| PRP         | 110| 2.2212 | 1.75120        | .16474          |
| Corticosteroids | 110| 3.8318 | 1.90573        | .18423          |

Table 9: t-test for Equality of Means

| AT Injection | Mean Difference | Std. Error Difference | Sig. (2-tailed) |
|--------------|-----------------|-----------------------|-----------------|
| Equal variances assumed | .051 | -.09974 | .5078 |
| Equal variances not assumed | .049 | -.09974 | .5045 |
| First month | Mean Difference | Std. Error Difference | Sig. (2-tailed) |
| Equal variances assumed | .101 | -.51195 | .3104 |
| Equal variances not assumed | .101 | -.51195 | .3105 |
| Second month | Mean Difference | Std. Error Difference | Sig. (2-tailed) |
| Equal variances assumed | .019 | -7.0300 | .2982 |
| Equal variances not assumed | .019 | -7.0300 | .2978 |
| Fourth month | Mean Difference | Std. Error Difference | Sig. (2-tailed) |
| Equal variances assumed | .000 | -1.18882 | .2516 |
| Equal variances not assumed | .000 | -1.18882 | .2521 |
| Sixth month | Mean Difference | Std. Error Difference | Sig. (2-tailed) |
| Equal variances assumed | .000 | -1.61054 | .2465 |
| Equal variances not assumed | .000 | -1.61054 | .2471 |

Our study was significant as the P value is <0.05

Discussion

Protease inhibitor, adhesive proteins, coagulation factors are the biologically active substances present in platelet for clotting. Platelets also release TGF –beta 1, VEGF, PDGF, CGF. These help in the process of tissue healing by cellular differentiation and proliferation, angiogenesis, tissue debris removal, chemotaxis, and ECM formation. By direct local injection of autologous platelet rich concentrate, degenerative conditions like tennis elbow are treated. Multiple methods are being used for the preparation of autologous Platelet Rich Plasma. The containers used for this preparation differs to minimize the direct blood-handling. The volume of Platelet Rich Plasma is usually 10 percent of the whole blood used. Alsousou J et al used a GPS system for preparation of PRP. The PRP volume of about 5 ml was collected following 12 minutes of rotations at 3200 rpm. Augustus D et al used a double centrifugation method which separates blood first into plasma and RBC. The Plasma formed was separated again in to Platelet Rich Plasma and platelet poor plasma by second centrifugation. In this study, Augustus D et al method of double centrifugation was used. By repeated trial and error method we standardized the procedure of preparation of platelet rich plasma. Platelet rich concentrate, autologous platelet gel are synonyms for platelet rich plasma. Platelet rich plasma is defined as autologous blood with a concentration of platelets above the base line values. The platelet counts in our samples ranged from two to six lakhs per cc. Hall M.P. et al described platelet rich plasma contains a two to eight fold increase in platelet concentration and 1-25 fold increase in growth factor concentration. According to Marx R E et al in an article “what is prp and what is not prp?” described that at least 10 lakhs of platelet per ml in five ml of plasma, will be associated with enhancement of healing. Alsousou J et al in a review article described a concentration of five times the normal count as working definition of PRP. ELISA can be used for measurement of concentration of the...
growth factors. Augustus D et al found that growth factors such as PDGF, IGF-1 will be increased in single centrifugation than in double centrifugation. Measurement of growth factors are not done because their assay was not cost effective.

Depending on WBC concentration, PRP classified as low WBC PRP and high WBC PRP. Augustus D et al found that WBC count is reduced in platelet poor plasma and increased in platelet rich plasma. There were no significant difference in WBC cell types in platelet poor plasma and platelet rich plasma. Some authors suggested avoiding exposure of WBC to tissues so that inflammatory reaction may reduce. Bielecki T M et al support the WBC presence as it increased release of growth factors and also has antibacterial actions.

After release from circulation, platelets in PRP get activated. Kenneth S Lee et al described that needle prick at the time of injection will induce bleeding which will provide the clotting factor thrombin needed for activating platelets. Addition of substances like bovine thrombin, calcium chloride and type I collagen for activating platelets.

Most of the authors used similar technique of infiltration for PRP treatment. Keith s Hetchman et al, Joost C Peerbooms et al, Ertugrul Akshin et al, Ehab Mohamed SlemRagab et al, used similar technique. They palpated the point of maximum tenderness and injected by single skin portal and five to six penetrations in surrounding tissues. This technique was known as peppering technique.

In our study, we used same technique for injecting platelet rich plasma in Tennis elbow patients. This was a prospective trial by study design conducted on 220 patients which includes 110 patients injected with PRP and 110 patients injected with corticosteroid injection.

Both groups of patients were selected based on the inclusion criteria and exclusion criteria described. Patients having chronic inflammatory conditions like rheumatoid arthritis are excluded from the study. Assessment of progression was done based on numerical pain scoring system.

Christos Thanases et al compared PRP to whole blood in the treatment for tennis elbow. Keith S Hetchman et al on 31 tennis elbow patients which was not responded for conservative treatment by single PRP injection.

Two parallel studies (PRP vs corticosteroid)

Samuel A Taylor et al on 100 tennis elbow patients compared between PRP and steroid injection. V V Reddy et al on 150 tennis elbow patients compared between PRP and corticosteroid. Both VAS and DASH score shows improvement in pain relief noted in PRP group compared than corticosteroid group at 26th and 52 weeks follow up.

On linking the results at 1,2,4,6 months of follow up, it was established that patients got relieved of their pain in one month. But, only at two months there was noticeable relief of symptoms. No patients had repeat injections. The above results were comparable with Ertugrul Akshin et al and Christos Thanases et al study.

The difference between 1, 2, 4 and 6 months pain reduction were tested for significance by paired T – test using SPS system. It was found that there was no notable difference in pain reduction between 2 months and 4 months, 2 months and 6 months, 4 months and 6 months scores. But there was major difference in pain score in 1 and 2 months. By testing independent samples T-test using equal variances assumed found that 2 months, 4 months and 6 months pain reduction was considerably equal in all groups.

Limitations of our study

1. A subjective evaluation was done based on patient’s insight of pain (VAS score) and the evaluation was not based on objective point of view (in the form of hand grip strength).
2. Control group was used and therefore available for evaluation in this study.
3. The concentration of platelets in PRP was not checked and standardized.

Summary

Lateral epicondylitis is considered to be a degenerative tendinopathy, with recurrent micro trauma as the major cause. Autologous platelet rich plasma injections and corticosteroid injections are gaining popularity in the treatment of tendinopathies such as tennis elbow. Platelet rich plasma contains growth factors which help in healing of tissues. We conducted a study by intralesional autologous platelet rich plasma injections and corticosteroid injections in patients with tennis elbow.

This was a prospective study conducted on total 220 patients, out of this 110 patients had autologous platelet rich plasma injection and 110 patients had corticosteroid injection for tennis elbow.

Patients were analyzed for percentage reduction of pain. Percentage reduction of pain is obtained by calculating the percentage of the difference of pain score at every follow up from initial pain score at the time of injection. Out of 220 patients, 110 patients given PRP and 110 patients Corticosteroids.

Based on inclusion and exclusion criteria patients were designated. Patients were given a single intralesional autologous PRP and corticosteroid injections by peppering technique. Platelet rich plasma was prepared by a double centrifugation method initially at 2500 rotations per minute for 10 minutes and later at 3500 rotations per minute for 15 minutes.

15ml of blood was withdrawn out of which 2ml of PRP was attained. Cell count was analyzed from this PRP. The initial and 1 & 2, 4, 6 month’s numerical pain score was recorded and analyzed.

In PRP group, 61 patients were male and 49 patients were female. Among male patients, based on VAS and DASH score 73% had excellent prognosis, 20% had good prognosis and 7% had poor prognosis. Among female patients, 82% had excellent prognosis, 14% had good prognosis and 4% had poor prognosis.

In Corticosteroid group, 61 patients were male and 49 patients were female. Among male patients, based on VAS and DASH score 36% had excellent prognosis, 59% had good prognosis and 5% had poor prognosis. Among female patients, 37% had excellent prognosis, 55% had good prognosis and 8% had poor prognosis.

In PRP group, among 58% of patients with right dominant side involvement, 40% of patients returned to their normal routine labourer work without any pain, rest 18% people started office works.

No correlation was found in the period of symptoms to pain relief which were assessed. On conclusion, it was found that intralesional autologous platelet rich plasma injection was safe and useful in the treatment of tennis elbow and provided better benefits on long term basis as compared to corticosteroid injection.

In our study, maximum benefit was observed at 2 months. One patient developed pain and swelling of right elbow after
2 months of PRP injection. On evaluation it was diagnosed to be biopsy proven tuberculous synovitis of elbow. He was started on Anti tuberculosis treatment. Subsequently patient recovered well.

Conclusion
Autologous PRP and Corticosteroid injection is a safe and useful modality of treatment in the treatment of lateral epicondylitis.
The response of patients with PRP was significantly better than Corticosteroid injection in the treatment of lateral epicondylitis.
Maximum benefit after PRP injection was observed at 2 months and sustained for at least 6 months.
Corticosteroids are effective on short term basis only. But PRP is effective on long term basis.
Also, we encourage more randomized clinical trials on this topic emphasizing on the number and frequency of injections as well as standardization of concentration of platelets in PRP to overcome limitations.
In our study, we found Autologous PRP is found to be superior than corticosteroid.

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