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Efficacy, safety and tolerability of autologous platelet rich plasma injection in the treatment of lateral epicondylitis

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ABSTRACT

Background: To evaluate the effects of platelet-rich plasma (PRP) infiltration in patients with lateral epicondylitis of the elbow.
Methods: A randomized, prospective study on 60 patients with lateral epicondylitis of the elbow was conducted at Ruby Hall Clinic, Pune. The patients were randomized and evaluated after receiving infiltration of three milliliters of PRP, or methyl prednisolone. The base-line evaluation was done using visual analog score (VAS) and modified Mayo performance index for elbow (MAYO). Re-evaluation was after 1 and 6 months of the procedure. Statistical analysis was done using independent t-test.
Results: After 6 months of treatment with PRP, patients with lateral epicondylitis had a statistically significant improvement in their VAS ($p<0.05$) in contrast to steroid. However, no statistical difference in modified Mayo performance index was found between the two groups at 1 and 6 months after intervention.
Conclusions: Treatment of patients with lateral epicondylitis with PRP reduces pain and is better tolerated than steroid therapy. Thus, the novel PRP therapy can be considered as a primary approach to treat patients of lateral epicondylitis conservatively.

Keywords: PRP, Lateral epicondylitis, Steroid, Elbow, Platelet

INTRODUCTION

Lateral epicondylitis (LE) or popularly called as Tennis Elbow with an annual incidence of 4– 7/1000, is the most common ailment affecting the elbow in the age group between 35 and 54 years.[1] It is commonly found in patients whose activities require strong gripping or repetitive wrist movements in the day-to-day activities of life.[2] The most commonly involved structure is the Extensor Carpe Radialis Brevis (ECRB) which attaches to the lateral epicondyle of the humerus. The other tendons which join the ECRB on the lateral epicondyle are extensor carpe ulnaris, extensor digiti mini and extensor digitorum.[3,4]

Pathological process commences with as a tear in the common extensor tendon caused by mechanical overloading and is followed by abnormal microvascular responses. The microscopic finding demonstrates immature tissue that resembles angiofibroblastic hyperplasia.[5] There is failure of the normal tendon repair mechanism associated with angiofibroblastic degeneration.

Several treatment modalities have been tried in management of epicondylitis such as nonsteroidal anti-inflammatory drugs, local anesthetics, botulinum toxin injection, physiotherapy, corticosteroid injections, extracorporeal shock wave therapy, autologous blood

constituents etc.[6-9] Corticosteroid injections remain the gold standard, but they do have limitation of short-term effect (2–6 weeks).[10]

Tendon regeneration may be improved by injecting autologous growth factors obtained from the patient's own blood. Autologous growth factors can be injected with autologous whole blood or platelet-rich plasma (PRP).

Autologous PRP delivered into various tissues to achieve a high local concentration of platelet-derived growth factors has been shown to enhance healing in wounds, tendons, and bones.[11] It is considered that supplementing the natural healing process with PRP would give better long-term results in the management of epicondylitis as compared to local corticosteroids. This study has been planned to evaluate the short-term and long-term outcomes of autologous PRP injection and corticosteroid injection in patients with lateral epicondylitis.

Objective of the study

The primary objective of the study was to evaluate efficacy of PRP in management of lateral epicondylitis. The secondary objective was to evaluate safety and tolerability of PRP in management of lateral epicondylitis.

METHODS

The study was initiated after obtaining study protocol approval by the Institutional Ethics Committee. All the patients or their guardians agreed to participate in the study through signing a free and informed consent statement, after having been given detailed information about the content and form of the study. The study was conducted at Ruby Hall Clinic, Pune.

The sample size was calculated before starting the study using SAS 9.2 package. The α and β risks (respectively 5% and 20%) and the variability of the variables (mean VAS steroid=4.69 and mean VAS PR=0.69, SD=4.6) were taken into account, and a minimum number of 26 participants per group was thus determined.[2] Considering the dropouts, actual sample size taken in each group was 30 patients.

Between 1st December 2018 and 1st June 2019, 75 consecutive patients with lateral epicondylitis of the elbow were selected for the study. The inclusion criteria were patient of either sex of age 18 to 70 years; diagnosed lateral epicondylitis; having platelet counts above 1.5 lakh/cumm and those who provided written informed consent.

The following patients were excluded: pregnant or nursing females; those who had undergone some form of previous treatment in the elbow region; those who presented other diseases in the upper limbs (such as posterior interosseous nerve syndrome and/or carpal tunnel syndrome, cervical radiculopathy); patients with systemic diseases (such as diabetes mellitus, hypothyroidism and/or rheumatoid arthritis); patients haemoglobin <10 mg/dl and on aspirin, or similar drugs.

The study duration was for 6 months (Individual patient). Patients received the treatment Platelet rich plasma or methyl prednisolone as per the randomization. Randomization chart was prepared by using SAS9.2 package.

The patients in steroid group were injected with methylprednisolone acetate 40 mg (1 ml) and lignocaine (1 ml) locally at the site of the tendon. The local infiltration was given by the peppering technique, wherein multiple injections were given at the most tender point of the elbow after changing direction so that maximum and effective infiltration could be achieved.[12]

Patients in the autologous PRP group had their platelet count done. Only those with counts above 1.5 lakh/cumm were selected for the study. A volume of 200 ml whole blood was collected in a standard 350 ml blood bag after removal of 21 ml of anticoagulant from the blood bag. The blood was collected on a biomixer (Terumo Pempol D 601) for continuous running of blood. The bag were be kept at room temperature (20°C–24°C), and separation was carried out as soon as possible. The blood was centrifuged using a light/soft spin with 1400 rpm at 22°C for 10 min. The supernatant was expressed into the transfer bag intended for platelet storage. The tubing was sealed twice and cut between the two seals. This bag was further centrifuged at 20°C using a heavy spin with 3500 rpm for 10 min. The "platelet-poor plasma" was expressed out into another bag, and tubing was sealed. Some plasma was left along with the settled platelets. The product was kept stationary at room temperature for approximately 1 h. Platelets were then transferred to platelet agitator at 20–24°C. The prepared unit was inspected for swirling movement. The patient received 2 ml of PRP with 1 ml of Lignocaine.

The tendon infiltration procedure was carried out by a single person to minimize the personal variations in the injection technique. Patients were closely observed for any systemic side effect, especially the giddiness and syncope. All patients were advised to rest the elbow and limit use of the arm for next 24h.

Assessment and end points

The study period was of 6 months for individual patient. There were 3 visits: Visit 1 on Day 1, Visit 2 on Day 30 and Visit 3 on end of 6 months (±1 week) (completion of the study). The improvement in pain was graded based on the quantum of change in the visual analog score (VAS) score and modified Mayo performance index for elbow (MAYO) on Day 0 (baseline), end of 1 and 6 months. During these visits general examination, assessment of pain and elbow function, global assessment of efficacy

by doctor and tolerability by patient, and capturing of any adverse event was carried out. Any investigations done were at the discretion of treating doctor and protocol did not require any additional investigation to be done

Primary endpoint was change in pain score on the visual analogue scale from baseline to end of one month. The secondary endpoints were: change in pain score on the visual analogue scale and Mayo performance index for elbow from baseline to end of six months. Physician's global assessment of response to therapy (PGART) and patient's global assessment of tolerability to therapy (PGATT) on a 4-point scale of "excellent, good, moderate & poor was carried out. The drop-out rate was determined at the end of the trial. Adverse drug reaction after consumption of medicine were evaluated in all patients in terms of nature and severity.

Statistical methods

Data was analysed using SPSS V15.0 package (Statistical Package for Social Sciences, Version 15.0). Data was given as Mean±SD Number and Percentage was given for categorical data. Comparison of mean between 2 therapies was carried out by Student's unpaired t test for normal numerical data. Fisher Exact Probability test or Chi square tests were applied to compare percentages for categorical data between 2 Therapies. All statistical tests were two tailed. Alpha (α) level of significance was taken as p≤0.05.

RESULTS

After exclusion of patients as per the eligibility criteria, we had a total of 60 cases; 30 in each Group I (steroid) and II (PRP). None of the patients were lost to follow-up at the end of 6 months. Thus all 60 patients were included for analysis in the end.

Group I had 18 (60.0%) males and 12 (40.0%) females whereas group II had equal number of male and female candidates 15 (50.0%). The mean age of group I and II was 40.10±9.18 and 37.93±15.16 respectively.

The height and body weight of patients enrolled in both groups, had statistically no significant difference. Height of patients was 162.43±8.75 in steroid group and 163.80 ± 9.69 in PRP group. Body weight of patients was 64.87±14.41 in steroid group and 73.70±14.94 in PRP group.

Significant difference was observed by VAS Score between 2 therapies at Day 30 and Day 180. The PRP therapy had significantly low VAS score than steroid therapy. The mean VAS score of 5.47±1.0 of steroid group on admission to study improved to 4.43±0.94 at Day 30 and 3.73±0.83 by Day 180. Comparatively, 5.07±1.02 VAS score of patients assigned to PRP group improved to 3.93±0.74 at Day 30 and 3.23±0.82 by Day 180 (Figure 1).

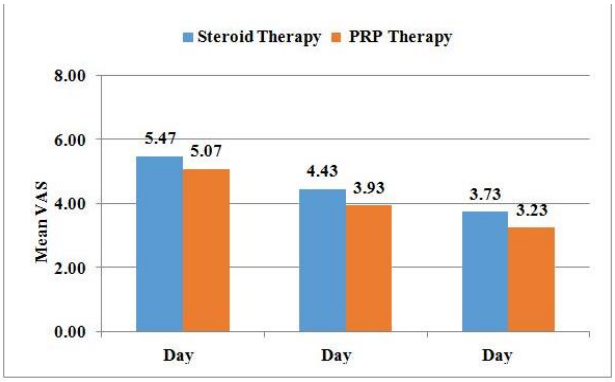

Figure 1: Comparison of mean VAS score of steroid group vs PRP group.

Table 1: Mayo index values of steroid group and group at Day 1, Day 30 and Day 60 (n=30).

Therapy	Steroid	PRP	t value, Sign, p value
Day 1	67.67±6.53	68.17±6.74	t=0.3, NS, p=0.8
Day 30	75.83±6.53	67.67±6.53	t=0.33, NS, p=0.7
Day 180	67.67±6.53	67.67±6.53	t=1.5, NS, p=0.15

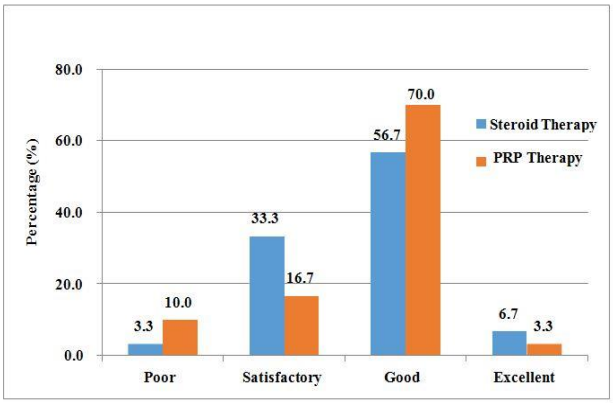

Figure 2: Physician's global assessment of response to therapy (%).

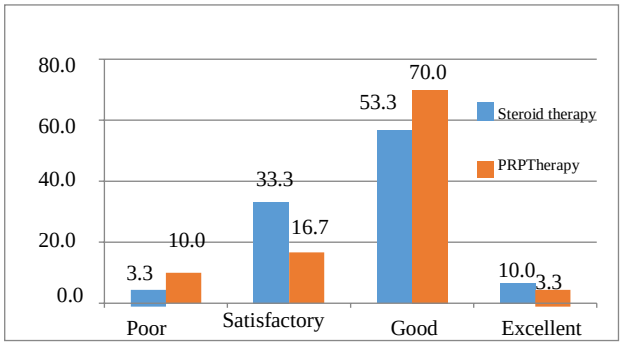

Figure 3: Patient's global assessment of tolerability to therapy (%).

The patient assessment by Mayo index values however shows no significant difference in the results obtained by either treatment. Both therapies had comparable values at all-time points. Patients under both therapies were evaluated by subjective assessment by the patient themselves and objective assessment by the doctor (Table 1). Both assessments graded the response and results obtained by therapy as poor, satisfactory, good, and excellent.

Patient's improvement under both therapies was also measured by physician's global assessment of response to therapy (PGART) and patient's global assessment of tolerability to therapy (PGATT). No significant difference between 2 Therapies was noted as per either PGART or PGATT (Figure 2 and 3).

Three incidences of treatment related complications were reported by steroid group as opposed to two in case of PRP group. The steroid group subjects reported local itching was 2 (6.7%) and local erythema was 1 (3.3%); whereas PRP group complained of local itching was 1 (3.3%) and nausea was 1 (3.3%).

DISCUSSION

Lateral epicondylitis was first described by Runge in the year 1873. It occurs equally in both gender, in 30-50 age group affecting between 1% and 3% of the population.[13] Presenting symptoms are painful and tender outer elbow. The gradual onset pain may extend to extensor compartment of forearm. Common initial therapy is rest, bracing, and NSAID. These therapies have limitations and only 87% patients respond to it.[6]

Surgical intervention is considered for recalcitrant cases, but for less severe cases, traditionally steroid therapy was implemented.[14-16] The patients are often unwilling for surgical intervention and demand for symptom relief only.[17,18]

In the current study, steroid therapy is compared with PRP therapy, a new innovative approach. It promises to overcome complications of both surgical and steroid therapy. The steroid therapy is not effective in terms of long term results.[19] Repeated steroid injections are associated with skin problems such as hypopigmentation and fat atrophy leading to indentation of the skin around the injection site.[20]

In a randomised controlled trial, corticosteroid injection proved to be best option only for short term. Repeat injection could not control relapse and led to permanent structural changes.[7].The studies involving steroid therapy, till date have been unable to formulate optimal timing, dosage, injection technique, and injection volume.[10]

Patients with platelet count above 1.5 lakh/cumm were included in PRP therapy group. The steroid and PRP have dissimilar effects at the site of injection. The PRP increases concentrations of autologous growth factors and secretory proteins at the site of tendinitis. These improve revascularization and enhances healing at the microscopic level. Whereas corticosteroids are synthetic drugs that closely resemble cortisol, a natural adrenal hormone. At the site of injection, steroid decrease inflammation and reduce the activity of the immune system. PRP therapy has been proved beneficial and superior in earlier studies.[9]

In a randomised control trial, 90% of patient had 25% reduction in their worst pain score. They were maintained without any further intervention for a pain free period of one year.[21]

The present study randomised patients to PRP and steroid therapy. Both groups had comparable Mayo Index but PRP group patients reported significantly low VAS score both at Day 30 and Day 180. Both therapies had equivalent doctor and patient's assessment. Initial results of steroid therapy were not sustained but PRP group presented gradual improvement in the initial positive findings. No Significant difference between 2 Therapies was noted as per either PGART or PGATT. Only minor complains like local itching, erythema and nausea were reported. Either therapy had no serious adverse events.

CONCLUSION

The study results indicate that single injection of autologous PRP achieve better functional and pain management as compared to steroid therapy. But the study cohort was small and was followed for a period of six months only. Thus the novel PRP therapy can be considered as a primary approach to treat patients of lateral epicondylitis conservatively.

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