

Treatment of Refractory Lateral Epicondylitis of Humerus with Local Autologous Plasma Injection

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Abstract

Introduction: Elbow lateral epicondylitis is a common problem that usually resolves with conservative treatment modalities such as local infiltration with steroids, ultrasonic therapy, manipulation, and finally operative procedures are tried. An alternative to surgical intervention is sought for when the conservative measures fail.

Purpose: The hypothesis of this study is to establish the role of local autologous plasma injection to bring along biological cure in these cases.

Materials and Methods: A total of 40 patients (40 elbows) with persisting pain for approximately 6 months, despite another conservative mode of intervention, were treated. The patients were injected with 2cc autologous plasma locally at the site of epicondylitis aseptically after preparation by centrifugation of 5cc blood. A post procedure physiotherapy program with an active range of exercises was followed in every patient. The outcome was rated by post procedure visual analog pain scores (VAS) and Mayo elbow performance scores (MEPSs). Informed consent had been obtained from the subjects, and the study protocol was approved by the institutional ethics committee.

Results: All patients in this study noted improvement in their VAS and MEPS. Minimal complication occurred in some patients. Mean VAS improved from 74.9 to start with to 41.5 at 4 weeks, 29.8 at 8, and 18.5 at 6 months follow-up. Mean MEPS improved from 50.3 to start with to 71.8 at 4 weeks, 79.7 at 8 weeks, and 84 at 6 months follow-up.

Conclusion: The treatment of patients with refractory lateral epicondylitis with local autologous plasma reduced pain significantly. Hence, local autologous plasma injection is a viable option to be considered before contemplating surgical intervention in refractory lateral epicondylitis of humerus.

Key words: Autologous plasma, Refractory lateral epicondylitis, Tennis elbow, Tendinitis, Tendinosis

INTRODUCTION

The lateral epicondylitis (tennis elbow) is a familiar term used to describe myriad symptoms along with activity-related pain around the lateral aspect of the elbow, with a common age of onset of 35-50 years and affecting around four adults/1000 annually. Activities requiring supination and pronation movements in near full elbow extended position leads to lateral epicondylitis of humerus.¹

Lateral epicondylitis is initiated by micro tear, most often, in the origin of the extensor carpi radialis brevis. The chronic overuse injuries following multiple micro traumatic events cause disruption of the internal structure of the tendon and degeneration of the cells and matrix. These fail to mature into normal tendon, at times, leading to tendinosis.² The term tendinitis is used frequently to describe these conditions, but histopathological studies have shown that specimens of tendon obtained from areas of chronic overuse do not contain large numbers of macrophages, lymphocytes, or neutrophils.^{3,4} The histopathologically tendinosis has been found to be a population of fibroblasts, vascular hyperplasia, and disorganized collagen which is termed as angiofibroblastic hyperplasia.⁵ Tendinitis, on the contrary, is characterized by the presence of an increased number of lymphocytes or neutrophils.

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The cause of tendinosis to be painful is unclear, and the cause of failure of collagen maturation is unknown. Tendons that are susceptible to injury are those that are involved in locomotion and ballistic performance, transmitting loads under elastic, and eccentric conditions.^{2,3,6} Tendons, wrapping around a convex surface or the apex of a concavity, those crossing two joints, those with areas of scanty vascular supply, and those that are subjected to repetitive tension and are susceptible to overuse injuries.^{4,7-10}

The cyriax noted in his study that the origin of the extensor carpi radialis brevis was the primary site of this injury, and histopathological changes have been documented at this location.^{4,10,12} Involvement of the origin of the extensor digitorum communis is also found in one-third of patients.^{4,12,13} If it is assumed that tendinoses have basically the same pathogenesis, then the biologic methods of the treatment of patients with tennis elbow can serve as a method for the treatment of pain in other regions in which tendinoses have been reported, such as the patellar ligament, the rotator cuff, the flexors and extensors of the elbow, the adductors of the hip, the triceps, the plantar fascia, and the achilles tendon. The plasma probably helps recruit bone marrow-derived stem cells to the site of injection and plasma-derived growth factors moderate the microvascular environment leading to the healing process. Further study into the mechanism of action of local autologous plasma is needed.

We chose to study lateral epicondylitis because it is clinically a very common entity and greatly hampers activities of daily living. Our hypothesis is that local autologous plasma injection in the treatment of cases of refractory lateral epicondylitis of humerus promotes biological healing and yield better functional results.

MATERIALS AND METHODS

The study was conducted in the Department of Orthopaedics, Medical College and Hospitals, Kolkata on a prospective basis from February 2014 to July 2015. Out of the patients attending the outpatient Department of Orthopaedics, Medical College and Hospitals, Kolkata and diagnosed as suffering from lateral epicondylitis of humerus, 40 patients were selected who fitted our criteria for the study. A written consent was obtained from all the patients. Inclusion criteria included adult patients (age group 20-60 years) suffering from lateral epicondylitis of humerus (after confirmation of diagnosis), pain persisting for at least 6 months and failure of conservative therapy including rest, activity modification, bracing, physiotherapy, steroid injection, and non-steroidal anti-inflammatory medication.

Exclusion criteria included pregnancy, presence or history of carpal tunnel syndrome, cervical radiculopathy, significant intra-articular pathology, lateral collateral ligament injuries, and systemic disorders such as diabetes, rheumatoid arthritis, and hepatitis. In all cases, patients complained of significant persistent pain that interfered with normal activities of daily living including combing hair, wrenching clothes and toileting, etc.

Every patient was assessed thoroughly and a detailed history of the patient was taken, noting the duration of pain, the mode and severity of injury, if any, and detailed examination of the affected part. A case included for the study was then again thoroughly examined. The case is again evaluated to confirm the diagnosis using the several tests for tennis elbow, such as extending the fully pronated and flexed elbow, Thompson's test, Mill's Maneuver and Cozen's test. The elbow tendinosis is diagnosed by physical examination and diagnostic imaging. Anteroposterior and lateral projection of radiographs of the affected elbow were checked in all cases to exclude obvious pathology of trauma or cubital tunnel osteophytes. Collateral ligament injury and neuritis were excluded by clinical or imaging studies. Sonographic scanning was used for the evaluation of tendon and ligament condition. All the patients were evaluated by visual analog pain scale (VAS) and Mayo elbow performance scores (MEPSs). The plasma for injection was prepared in the Institute of Haematology and Transfusion Medicine, Medical College and Hospitals, Kolkata.

After proper counseling and following aseptic precautions, about 5cc of blood was drawn in a syringe containing 0.5 cc of heparin from the patient's contralateral forearm vein. The drawn blood was then transferred to a pre-sterilized centrifuge tube. The blood was centrifuged at 1300 rpm for approximately 20-25 min to generate the plasma. Of the centrifuged plasma, only the clear upper layer and the buffy coat layer that contained mononuclear cell were used for injection. The duration from drawing of blood and injecting the plasma was between 30 and 45 min.

The patients were placed in the supine posture with the arm fully adducted at the patient's side, and the elbow flexed to 45° with the wrist dorsiflexed passively using a sand bag to relax the affected tendons in pronation. In this position, the lateral epicondyle and the most tender point is identified. The local area is then painted and draped adequately. The disposable syringe with 22-gauge needle was advanced perpendicular to the lateral epicondyle through the skin till it touches the bone. The needle is then slightly withdrawn by 1-2 mm and approximately 2.5 mL of autologous plasma was injected directly into the area of maximum tenderness and into the common extensor tendon origin and undersurface of extensor carpi radialis brevis. The technique involved a single skin entry and then

5 penetrations of the tendon.

Immediately after the injection, the patient was kept in a supine position without moving the arm for 15 min. The patients were sent home with a compression bandage and instructions to limit their use of the arm for approximately 24 h and use oral nonsteroidal anti-inflammatory drugs for 3 days for pain and local ice pack if required. After 24 h, patients were given a standardized stretching protocol to follow for 2 weeks. The patients were told to continue activities of normal daily living but to avoid any activities that were likely to aggravate symptoms. A formal strengthening program was initiated after this stretching. At 4 weeks after the procedure, patients were allowed to proceed with normal activities as tolerated. The patients were examined at 4 weeks, 8 weeks, and 6 months after the procedure. On every follow-up visit, the patients were examined thoroughly.

MEPS system is the most widely used scoring system in cases of analysis of elbow pathology. It provides a good analysis of the functional outcome of procedures done around the elbow. Hence, we used the MEPS for analyzing our results. A 100 mm VAS (0=no pain; 100 worst pain possible) with color coding is used to evaluate the subjective interpretation of pain.

The changes in the mean values of the MEPS and the VAS from the pre procedure to each follow-up level were assessed by analysis of variance (ANOVA). Statistical analysis is performed using Student's *t*-test, Chi-square test, and standardized statistical package.

RESULTS

The patients ranged from 26 to 56 years (average 41.4 years). The most frequent age group affected was 30-39 years. They all underwent injection procedure and were followed up in this hospital on outpatient basis for a period ranging from 6 to 14 months (average 8 months). 18 among the 40 patients were males and 22 among them were females. Sex distribution can be stated to be equal in incidence. Among the 40 patients, 21 were housewives, 9 were farmers, 9 were daily laborers, and 4 were desktop workers. Among the 40 patients selected, in 28 the dominant upper limb was affected and in 12 the non-dominant side was affected.

The presence of pain was graded as none, mild, moderate, and severe; 33 out of the total 40 cases (82.5%) had moderate pain and 7 out of 40 (17.5%) had severe pain at the pre procedure level. At 6 months follow-up, 8 out of 40 (20%) had "none" pain, 30 out of 40 (75%) had mild pain, and 2 out of 40 cases (5%) had moderate pain. The function to comb hair improved from 10 out of 40 cases (25%) pre procedure to 36 out of 40 cases (90%) at

6 months follow-up; feed self-function improved from 31 out of 40 cases (77.5%) pre procedure to 39 out of 40 cases (97.5%) at 6 months follow-up; hygiene function improved from 19 cases (47.5%) pre procedure to 38 cases (95%) at 6 months follow-up; dressing function improved from 1 case (2.5%) pre procedure to 33 cases (82.5%) at 6 months follow-up; finally, shoe function improved from 2 cases (5%) pre procedure to 23 cases (57.5%) at 6 months follow-up. Initially, the patients selected for the study had a mean Mayo elbow score of 50.25; which at 4 weeks follow-up showed a mean of 71.75; at 8 weeks follow-up showed a mean of 79.75 and at 6 months follow-up improved to 84. Result interpretation based on MEPS showed improvements as excellent in 7, good in 29, fair in 3, and poor in 1.

Initially, the patients selected for the study had a mean VAS of 74.9; which at 4 weeks follow-up showed a mean of 41.5; at 8 weeks follow-up showed a mean of 29.8 and at 6 months follow-up improved to 18.5.

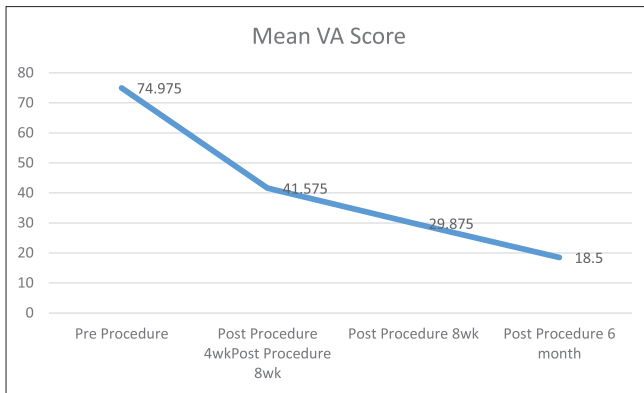
A graphical representation of the mean VAS and mean MEPS respectively from pre procedure status to 6 months post procedure follow up is given in Graphs 1 and 2.

The changes in the mean values of the MEPS and the VAS from the pre procedure to each follow-up level were assessed by ANOVA. Based on the results of the above-mentioned statistical analyses, we concluded that the difference we obtained between the modalities of evaluation was statistically significant ($P < 0.0001$).

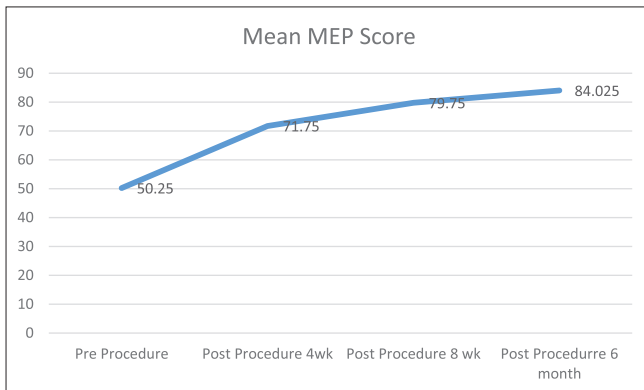
Pain (moderate) with associated functional difficulties persisted in 2 (5%) cases. Severe pain was not present in any cases at 6 months follow-up. No other cases had any other complications of infection, local skin condition changes, and neurovascular deficit distally. 24 patients complained of increased pain following injection procedure, which was relieved with analgesics and local ice pack application within 5 days.

DISCUSSION

The lateral epicondylitis of humerus is a common problem usually controlled by conservative modalities. If conservative methods do not provide satisfactory remedy, other options are tried. A meta-analysis of physical therapy, recently, failed to provide evidence to establish it as a treatment modality providing long-term relief.¹⁴ The physical therapy, though, is also used in our study in the post procedure stretching and strengthening exercises. Corticosteroid injections have been used most popularly and extensively for treatment, but studies have raised certain doubts about their efficacy.^{15,16} The superficial injection of corticosteroid may result in



Graph 1: Mean visual analog score



Graph 2: Mean Mayo elbow performance score

subcutaneous atrophy and sometimes leading to permanent ultrastructural changes following intratendinous injection, as observed by Jobe and Ciccotti.¹⁷ In our study, this sort of complication did not occur as this is a biologic form of treatment. Extracorporeal shock wave therapy was shown to be no better than placebo in a recent study.¹⁸ In this day, orthopedics biological treatment modalities are gaining popularity. Bone morphogenic proteins and other growth factors have been studied *in vitro* and presently are being tested *in vivo* also.¹⁹ Autologous plasma may also be helpful for wound healing. The study by Edwards and Calandruccio²⁰ showed that 22/28 patients responded to autologous blood injections, with average MEPS decreasing from 6.5 to 2.0 after a mean follow-up of 9.5 months. They, using whole blood, noted a 79% success rate when treating lateral epicondylitis. We used autologous plasma instead of blood to decrease the volume of injection and also to avoid the deposition of iron locally following breakdown of red blood cells if any. Mishra *et al.*²¹ introduced buffered platelet rich plasma technique in the treatment of chronic elbow tendinosis. Moon *et al.*²² concluded that the injection of iliac bone marrow plasma after arthroscopic debridement in severe elbow tendinosis demonstrated early recovery of daily activities and clear improvement. Klein *et al.*²³ reported in their study that transforming growth factor

beta increases Type I collagen production in tendon sheath fibroblasts. These mechanisms may be at work in our study also. Further study into the mechanisms by which plasma works is needed. We chose to study lateral epicondylitis of humerus because it is clinically very common and hampers activities of daily living. In this study, the patients treated with plasma did significantly better at 4 weeks and 8 weeks. At 6 months after treatment, however, the autologous plasma injected patients improved from a mean VAS of 74.9 at pre procedure level to 18.5 at 6 months follow-up and a mean Mayo elbow pain score of 50.25 at pre procedure level improved to 84 at 6 months follow-up. Of importance, no plasma treated patient was worse after treatment. Two out of 40 cases (5%) had residual moderate pain, and there were no significant complications in this study. Although, there were some problems with some patients in explaining the methodology and post procedure protocol. The limitations of this study include lack of a randomized control group and the small number of patients. Further study of autologous plasma versus whole blood or cortisone should also be performed in the future.

CONCLUSION

The data suggest autologous plasma may be an alternative to surgery in patients with this disorder or of its kind. Hence, to conclude, the use of autologous plasma injection method provides biologic healing and is an effective solution for refractory lateral epicondylitis of humerus and similar disorders.

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