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MRI correlation of tennis elbow patients treated with platelet rich plasma (PRP)

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Abstract

Introduction: Tennis elbow is a common problem, for which current available treatments are often unsatisfactory. Biologic therapies, such as platelet rich plasma (PRP) injections, aimed at stimulating healing of degenerative tendons by releasing growth factors, have shown promise *in vitro* study but clinical research is limited. The objective of present study is to study the efficacy of platelet rich plasma in tennis elbow, and to evaluate the outcomes of this recent modality of treatment for tennis elbow by MRI studies.

Materials and Methods: Patients who were diagnosed with tennis elbow and undergone conservative treatment for at least 3 months but not improved were included in the study after obtaining written informed consent. After preparation of PRP by centrifugation, the injection was given under ultrasonography (USG) guidance at the site of tendinopathy within 4 hours of preparation. The patients were evaluated by Magnetic Resonance Imaging (MRI) pre procedure and post procedure at 1 week, 1, 2, 3, and 6 months.

Result: 30 patients fulfilling the inclusion criteria were included in the study and treated with PRP. Majority of them showed significant improvement in terms MRI studies and were able to return to work at 6 months of follow up.

Conclusion: Platelet-rich plasma (PRP) may represent a therapeutic option for tennis elbow. Thus, future research should focus on identifying proper treatment time, optimal dosage and ideal PRP concentration.

Keywords: Platelet rich plasma, magnetic resonance imaging, tennis elbow

Introduction

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 [1, 2]. The frequency of lateral epicondylitis is reported between 1 to 3% among normal non-athlete population [3]. 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 termed "angiofibroblastic hyperplasia" [1, 2]. It causes pain and functional impairment in daily activities [2, 3]. The treatment of this condition includes conservative therapy and surgical interventions [3, 4]. The effectiveness of oral non-steroidal anti-inflammatory agents, topical and injectable medications including corticosteroids and botulinum toxins, splinting, physical therapy, and iontophoresis has been evaluated in many studies [4]. However, these traditional therapies do not alter the tendon's inherent poor healing properties secondary to poor vascularization [5, 6]. Given the inherent nature of the tendon, the treatment options including platelets rich plasma (PRP), autologous blood, and prolotherapy are aimed at inducing inflammation rather than suppressing it [7-9]. PRP is quite a good treatment used for chronic tendinitis [4]. PRP contain platelets, and these platelets have strong growth factors and granules that have critical role in the healing process of chronic injuries [7, 8]. 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 nonhealing tendinopathies including tennis elbow [4, 8, 9]. Therapeutic PRP should have a platelet concentration 3 to 6 times greater than that of whole blood (200000/mm3).

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The concentrations less than or greater than this amount may be ineffective or inversely lead to suppression of the healing process [4, 6, 7]. Some studies have shown that local injection of autologous whole blood has greater therapeutic effect than steroid injection in treating tennis elbow [5, 10, 11]; also there are studies showing the greater efficacy of local autologous PRP than corticosteroids in treating this disorder [4, 8]. However, only a few studies have been conducted to compare the efficacy of these two treatments. A comparative study of these 2 treatments was conducted by Thanasas et al. in 2011 in an effort to investigate the possible advantages of PRP versus autologous whole blood for the treatment of chronic tennis elbow. Six weeks after the therapy, PRP treatment seemed to be more effective than autologous blood in reducing pain [12]. However, this study and most of the other similar studies lacked objective evaluations of symptom improvements after whole blood or PRP injection. Considering the lack of a study of PRP injection objectively, the aim of the current study was designed to evaluate the effect of PRP injection in chronic tennis elbow which had not improved with conservative treatment.

Materials and Methods

This was a prospective study undertaken in a tertiary care hospital where patients with lateral epicondyle tendinopathy were included in the study after obtaining their informed consent. This study was undertaken from April 2016 to April 2018 after obtaining permission from Institutional Ethical Committee. Chronic lateral epicondylitis is defined as lateral epicondvlitis symptoms that last for more than 3 months [13]. But in this study Patient with symptoms typical of chronic tennis elbow who had taken drugs like paracetamol 500mg or ibuprofen 200mg thrice a day, activity modification in terms of avoiding lifting of heavy weight, rest and physiotherapy in terms of extracorporeal shock wave therapy for 3 months but pain not decreased in terms of VAS and MEPS or pain increased than before were included in this study. A detail history was obtained for evaluating the mode of trauma, visual analogue score, chronicity, physiotherapy, any injection taken previously etc. Detail clinical examination and x-rays were obtained to see any evidence of fracture. Laboratory investigations were carried out in all patients which include complete blood count (CBC), erythrocyte sedimentation rate (ESR), random blood sugar (RBS), radiograph of elbow and ultrasonography of local part before giving injection. Magnetic resonance imaging (MRI) was conducted in only all patients for diagnosis and study purpose. Blood count was done to see white cell counts to rule out infection, ESR was also done to rule out infection, RBS done to check for diabetes, radiographs done to rule out fracture and ultrasonography was done to see for the degenerative changes. The diagnosis was based on (1) pain over the lateral

humeral epicondyle that may radiate distally to the forearm, (2) tenderness over lateral humeral epicondyle and (3) aggravated pain on gripping, lifting and resisted wrist and/or second or third finger extension. If these three features were present for more than 3 months with or without conservative treatment as mentioned above, then only patients were included in the study. Patients who were having any skin pathology at the injection site, patients having symptoms of tennis elbow with less than 3 months of duration, patients who were on antiplatelet therapy like myocardial infarction, stroke, pregnancy, etc. and patients who were having more than one tendinopathies were excluded from the study. After taking written consent from the patient, around 40 ml blood was withdrawn by venepuncture in acid citrate dextrose (ACD) tubes with help of scalp vein. Platelet count was checked in the sample. The sample was centrifuged in machine using a soft spin at 3000 rotation per minute. Supernatant plasma was then transferred to another sterile tube without containing any anticoagulant. Centrifuge this tube at a higher speed using a hard spin. After that the lower 1/3rd was platelet rich plasma (PRP) and upper 2/3rd platelet poor plasma (PPP). At the bottom of the tube, platelet pellets were formed. Suspend the platelet pellets in a minimum quality of plasma after removing PPP and then gently shake the tube. The platelet count is checked and it should contain 3 to 5 times of platelet count from its baseline. This platelet rich plasma was injected within 4 hour of preparation under ultrasonography guidance at the site of pain with aseptic precautions. After giving platelet rich plasma injection, patients were given paracetamol 500mg thrice a day and arm sling for 4 weeks. MRI images were taken post 1 week after the procedure during 1st follow up. All the patients were followed up in OPD (outpatient department) at 1 week, 1 month, 3 months and 6 months. At every follow up, range of motion, visual analogue scale, Mayo elbow performance score and local complications were recorded along with the duration at which patient joined back to duty after PRP injection.

Results

The pre-treatment MRI findings noted that 9 (30%) patients had mild Tendinosis while 15 (50%) and 6 (20%) patients had moderate and severe Tendinosis respectively. Also partial thickness tears were present in 15 (50%) patients while 15 (50%) patients had no tears. There was significant improvement in patients during the follow-up period. The post-op 6 months MRI findings noted that 25 (83.3%) patients had mild Tendinosis while 3 (10%) and 2 (6.7%) patients had moderate and severe Tendinosis respectively (p<0.05). Partial thickness tears were present in 5 (16.7%) patients while 25 (83.3%) patients had no tears.

Table 1: Comparison of MRI findings of patients

MRI Findings	Tendinosis			Tear	
	Mild	Moderate	Severe	Partial	No
Baseline	9 (30%)	15 (50%)	6 (20%)	15 (50%)	15 (50%)
Post-op 1 Week	11 (36.7%)	13 (43.3%)	6 (20%)	13 (43.3%)	17 (56.7%)
Post-op 1 Month	14 (46.6%)	11 (36.7%)	5 (16.7%)	11 (36.7%)	19 (63.3%)
Post-op 2 Months	18 (60%)	8 (26.7%)	4 (13.3%)	9 (30%)	21 (70%)
Post-op 3 Months	21 (70%)	6 (20%)	3 (10%)	7 (23.3%)	23 (76.7%)
Post-op 6 months	25 (83.3%)	3 (10%)	2 (6.7%)	5 (16.7%)	25 (83.3%)

Discussion

A hospital based analytical study was conducted to evaluate

pathophysiology and outcome of 30 patients treated with PRP injections in tennis elbow and study the MRI findings.

Lateral epicondylitis or tennis elbow is a pathologic condition of the CET. The accepted cause is tendon injury often secondary to repetitive contractions of the forearm extensor muscles. This leads to disruption of the internal structure of the tendon and degeneration of the cells and matrix, which ultimately leads to macroscopic tear and tendon failure. Diagnosis of lateral epicondylitis is often made clinically; patients exhibit a continuum of symptoms that range relatively mild, yet persistent, annoyances during daily activities to severe and significantly limiting symptoms in all most facets of life. There have been many outcome measures to stratify patients according to their symptom such as the visual analog scale (VAS), the Disabilities of Arm, Shoulder and Hand (DASH) Questionnaire, and the Upper Extremity Function Scale (UEFS).

The appearance of tendinopathy in lateral epicondylitis on MRI includes an increased signal within or around the CET, tendon thickening, and a discrete collection of fluid between the lateral collateral ligament. The series by Chen J *et al.* [1] and Steinborn M *et al.* reported that MR assessment of lateral epicondylitis correlated well with surgical and histologic findings. Some previous studies have demonstrated that individuals with diagnosis of lateral epicondylitis are statistically more likely to have signal changes on MRI than that of controls. This is also confirmed by a meta-analysis study showing that ~90% of patients with lateral epicondylitis had abnormal signal in CET of affected elbows compared with 14% of controls.

In the present study, majority of the patients (40%) were from the age group of 31-40 years followed by 26.7% from the age group of 41-50 years, 20% from the age group of 51-60 years and 13.3% from the age group of 21-30 years. The mean age of patients was 40.63 ± 9.96 years. There were 20 (66.7%) male patients and 10 (33.3%) female patients in our study. This is similar to the studies of Halpern B et al. Qi L et al. and Khaliq A et al. Halpern B et al. prospective case series investigating Platelet Rich Plasma (PRP) treatment of elbow tendinosis association with improved clinical outcomes with respect to pain, function and return to sports/ recreation and determine if an MRI would detect any significant structural changes of the tendon after treatment found average age of patients was 51.9 years with 43% females (N = 49) and 57% males (N = 65).Qi L et al. study determining the interreliability and intra-observer reliability of magnetic resonance imaging (MRI) for lateral epicondylitis and investigating whether there is a potential relationship between MRI abnormalities of the common extensor tendon (CET) and its clinical symptom found 46 men and 50 women with a mean age of 46.2 years (range, 23–51 years).

Khaliq A *et al.* randomised controlled study comparing the treatment modalities of lateral epicondylitis in terms of pain relief found 102 patients divided into two groups of 51(50%) each. The over mean age was 33.9±10.3 years. Mean age of patients in the corticosteroid group was 34.2±10.2 years and in the other group it was 33.6±10.5 years. In our study, there was dominance of right side (70%) as compared to left side (30%). This is consistent with the study of Qi L *et al.* Qi L *et al.* study determining the inter-reliability and intra-observer reliability of magnetic resonance imaging (MRI) for lateral epicondylitis found 96 elbows (66 right, 30 left) in 96 patients.

t was observed in our study that the duration of symptom in 5 (16.7%) patients was <1 month while the duration of symptom in 15 (50%) and 10 (33.3%) patients was 1-2 months and >2 months respectively. The mean duration of

symptom in patients was 1.97 ± 0.91 months. This finding was consistent with the study of Qi L *et al.* Qi L *et al.* study determining the inter-reliability and intra-observer reliability of magnetic resonance imaging (MRI) for lateral epicondylitis and investigating whether there is a potential relationship between MRI abnormalities of the common extensor tendon (CET) and its clinical symptom reported average total duration of symptoms was 1.6 years (range, 6 months to 3 years).

It was observed in the present study that 5 (16.7%) patients had diabetes mellitus while 3 (10%) patients had hypertension. The mean baseline VAS score was 7.63 ± 0.50 which decreased to 5.81 ± 0.73 in post-op 1 week with mean difference of 1.82. This difference was statistically significant as Student t-test (p<0.05). Similarly the VAS score reduced significantly in post-op 1 month, post-op 2 months, post-op 3 months and post-op 6 months follow-up period. This is comparable to the studies of Halpern B *et al.* Bobin Mi *et al.* and Khaliq A *et al.*

Halpern B *et al.* prospective case series investigating Platelet Rich Plasma (PRP) treatment of elbow tendinosis association with improved clinical outcomes with respect to pain, function and return to sports/ recreation and determine if an MRI would detect any significant structural changes of the tendon after treatment reported 61% reduction in mean baseline VAS pain scores was seen at six months (from 3.914 to 1.514, p<0.001), a 69% improvement at 1 year (3.818 to 1.182, p<0.001, and an 83% improvement at 2 years (p<0.001). At 2 years, 41 out of 43 patients (95%) showed at least a 25% decrease in VAS pain scores. However, there was no significant difference in VAS pain scores between 6 to 12, and 12 to 24 months (p>0.05).

Bobin Mi *et al.* meta-analysis of randomized clinical trials comparing the effectiveness of platelet rich plasma (PRP) vs steroid in reducing pain and improving function of the elbow in the treatment of LE reported no significant difference in pain relief in the short-term (2 to 4 weeks: SMD = 1.02, P = .03; 6 to 8 weeks: SMD = .73, P = .24) and the intermediate-term (12 weeks: SMD = -0.28, P = .35). Steroid exhibited a better efficacy of function in the short-term (2 to 4 weeks: SMD = .61, P < .001; 6 to 8 weeks: SMD = .53, P < .001). However, PRP was superior to steroid for pain relief in the long-term (half year: SMD = -1.6, P < .001; one year: SMD = -1.45, P < .001), and also for function improving in the intermediate-term (12 weeks: SMD = -0.53, P < .001) and the long-term (half year: SMD = -0.56, P < .001; one year: SMD = -0.7, P < .001).

Khaliq A *et al.* randomised controlled study comparing the treatment modalities of lateral epicondylitis in terms of pain relief reported mean baseline visual analogue score in group A were 6.5 ± 1.2 and in group B it was 6.7 ± 1.4 . In group A, 74.5% of patients presented in moderate pain category and 25.5% presented in severe pain category. In group B, 70.6% presented in moderate with 29.4% presented in severe pain category. On follow-up, the mean pain score in group A was 4.0 ± 2.6 and in group B it was 3.5 ± 2.61 . Group A showed effectiveness in 52.9% patients and group B showed effectiveness in 82.3% (p=0.001).

In the present study, the mean baseline DASH score was 51.87 ± 6.30 which decreased to 46.28 ± 6.16 in post-op 1 week with mean difference of 5.59. This difference was statistically significant as Student t-test (p<0.05). Similarly the DASH score reduced significantly in post-op 1 month, post-op 2 months, post-op 3 months and post-op 6 months follow-up period. This is concordant to the studies of Thanasas C *et al.*

Halpern B et al. Lim W et al. Arik HO et al. Sampson S et al. Gosens T et al. and Qi L et al.

Thanasas C *et al.* randomized controlled clinical comparative study investigating the possible advantages of single injection of 3 mL of autologous blood and 3 mL of PRP under ultrasound guidance reported VAS score improvement was larger in group B at every follow-up interval but the difference was statistically significant only at 6 weeks, when mean improvement was 3.8 points (95% confidence interval [CI], 3.1-4.5) in group B (61.47% improvement) and 2.5 points (95% CI, 1.9-3.1) in group A (41.6% improvement) (P < .05). No statistically significant difference was noted between groups regarding Liverpool elbow score.

Halpern B *et al.* prospective case series investigating Platelet Rich Plasma (PRP) treatment of elbow tendinosis reported functional scores from baseline showed a 64% increase at 6 months (from 4.794 to 7.882, p<0.001), a 76% improvement at 1 year (4.722 to 8.333, p<0.001) and a 77% improvement at 2 years (p<0.001). Again, no significant difference was detected in functional scores between 6 to 12, and 12 to 24 months (p>0.05). A similar trend was seen for sport/recreational levels, with a mean improvement from baseline of 81% at 6 months (from 3.758 to 6.818, p<0.001), a 165% improvement at 1 year (2.824 to 7.471, p<0.001), and a 107% improvement at 2 years (p<0.001). Sports/recreational levels did not significantly differ between 6 to 12, and 12 to 24 months (p>0.05).

Lim W *et al.* study investigating the clinical effects of PRP and its biological components reported at 24 weeks, all pain and functional variables, including VAS score, Mayo Clinic performance scores, and MRI grade, improved significantly in group 1 (p < 0.05). PDGF-AB, PDGF-BB, and TGF- β levels were more significantly increased in PRP than in whole blood. TGF- β level significantly correlated with Mayo Clinic performance score and MRI grade improvement. Thus, TGF- β level in PRP is considered to play a pivotal role in tendon healing.

Arik HO et al. randomised controlled study comparing the efficacy of autologous blood injection versus corticosteroid injection for lateral epicondylitis reported no complications (infection, skin atrophy, neurovascular damage, or tendon rupture). 10 patients reported increased pain for up to 2 days after autologous blood injection. In both groups, the VAS score for elbow pain, PRTEE score, and grip strength improved significantly after treatment (p=0.0001), but the pattern of improvement differed. Compared with autologous blood injection, corticosteroid injection improved all 3 scores at a faster rate over the first 15 days (p=0.0001), and then started to decline slightly until day 90. After autologous blood injection, all 3 scores improved steadily and were eventually better (p=0.0001). If a 37% decrease in PRTEE is defined as complete recovery, 38 (95%) of patients with autologous blood injection and 25 (62.5%) of patients with corticosteroid injection achieved complete recovery (p=0.0001).

Sampson S *et al.* and Gosens T *et al.* double blinded randomized control trial evaluating the effects of PRP on chronic lateral epicondylitis in comparison to corticosteroid treatment reported successful outcomes as a 25% reduction in VAS or DASH scores without re intervention after one year. While both groups reported a significant improvement in symptoms, the PRP treatment was associated with a significantly greater 73% reduction in VAS scores compared to the 49% reduction associated with corticosteroid treatment. Qi L *et al.* study determining the inter-reliability and intra-observer reliability of magnetic resonance imaging (MRI) for

lateral epicondylitis reported median PRTEE score of all patients was 61 (range 8–98), the median PRTEE score of tendinopathy score 1 was 21, the median PRTEE score of tendinopathy score 2 was 45, and the median PRTEE score of tendinopathy score 3 was 86. PRTEE scores were gradually increased with the tendinopathy scores. Spearman's test showed a significantly positive correlation between tendinopathy scores and PRTEE scores (correlation coefficient r=0.920, P<0.01).

In our study, the pre-treatment MRI findings noted that 9 (30%) patients had mild Tendinosis while 15 (50%) and 6 (20%) patients had moderate and severe Tendinosis respectively. Also partial thickness tears were present in 15 (50%) patients while 15 (50%) patients had no tears. There was significant improvement in patients during the follow-up period. The post-op 6 months MRI findings noted that 25 (83.3%) patients had mild Tendinosis while 3 (10%) and 2 (6.7%) patients had moderate and severe Tendinosis respectively (p<0.05). Partial thickness tears were present in 5 (16.7%) patients while 25 (83.3%) patients had no tears. Similar observations were noted in the studies of Halpern B *et al.* Qi L *et al.* and Walton MJ *et al.*

Halpern B et al. prospective case series investigating Platelet Rich Plasma (PRP) treatment of elbow tendinosis association with improved clinical outcomes with respect to pain, function and return to sports/ recreation and determine if an MRI would detect any significant structural changes of the tendon after treatment reported Extensor tendinopathy (lateral epicondylitis) was diagnosed in 74 elbows and flexor tendinosis was found to affect 40 elbows based upon clinical symptoms and MRI evaluation. Seventeen patients underwent MRI prior to PRP treatment and at 6 or 12 months post PRPtreatment. On the pre-treatment MRI, 5 (29.4%) patients had mild tendinosis, 9 (52.9%) had moderate tendinosis, 3 (17.6%) had severe tendinosis. Additionally, partial thickness tears were present in 9 (52.9%) patients, while 8 (47.1%) patients had no tears Overall; there was a 47.1% (8 patients) improvement in the post-treatment MRI grading of tendinosis. While PRP appeared to have a greater effect on improving the MRI appearance of moderate and severe tendinosis rather than mild tendinosis. Of the 9 patients with partial tears at baseline, a repeat MRI 6-12 months after PRP treatment showed that 4 (44.4%) improved and 5 (55.6%) partials tears remained unchanged, suggesting that some partial tendon tears did improve on the post-treatment MRI, 2 (25%) patients who did not have tears at baseline developed tears between 6-12 months after PRP injections.

Qi L *et al.* study determining the inter-reliability and intraobserver reliability of magnetic resonance imaging (MRI) for lateral epicondylitis reported 96 elbows had MRI-assessed tendinopathy, that includes 38 (39.6%) with grade 1, 31 (32.3%) with grade 2, and 27 (28.1%) with grade 3. The average intra-observer agreement for grading the severity of tendinopathy was 77.3%. Weighted kappa values for intraobserver reliability were 0.762, 0.721, and 0.937 (P<0.001) for radiologists, respectively.

Walton MJ *et al.* study on relationship between MRI abnormalities of the common extensor origin and the patient's clinical assessment reported moderate or severe signal changes consistent with tendinosis were observed in 18 of 21 patients. Significant inter-observer reliability and intra-observer agreement were demonstrated for MRI interpretation of grade of tendinosis and length of tendon separation. Significant negative correlation was found between the length of tendon separation and both the Quick DASH and

maximum pain levels.

The optimum PRP formulation has not been identified. Different preparations systems produce varying PRP concentrations, cellular components, volumes, and utilize different activation techniques that make it difficult to compare clinical outcomes using different commercial systems.

Conclusion

PRP treatment seems to be an effective treatment regarding pain reduction for chronic lateral elbow epicondvlitis and superior to autologous blood in the short term. Defining details of indications, best PRP concentration, number and time of injections, as well as rehabilitation protocol might increase the method's effectiveness. Improved MRI appearance of tendinosis and partial tears was also detected in the subset of patients with follow-up MRIs. MRI is a reliable tool in determining radiological severity of lateral epicondylitis and can be reliably reported between observers on different occasions; MRI is also a valid tool in evaluating the clinical severity of lateral epicondylitis; the severity of MR signal changes of CET positively correlated with the patient's clinical symptoms. Additionally, the possibility of cost reduction of the method might justify the use of PRP over autologous whole blood for chronic or refractory tennis elbow.

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