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Treatment of lateral epicondylitis with autologous platelet rich plasma injection

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Abstract

Outcomes of traditional treatment methods of lateral epicondylitis are variable because of poor tendon healing properties secondary to poor vascularization. Platelet rich plasma provides locally high concentration of growth factors and have shown its efficacy in many tendinopathies and wound healing. We tried to measure the efficacy of locally injected autologous PRP, subjectively by functional oxford elbow score and pain score as well as objectively by ultrasonographic evaluation of the morphologic changes (focal hypoechoic, edema, tendon thickness, fraying, tear, cortical erosion, calcification) in common extensor origin in 30 patients with mean age of 39.3 years of recalcitrant lateral epicondylitis. The mean pain VAS Score improved from 7.7 before injection to 1.8 at final follow up i.e. after 6 months post injection. The Oxford elbow score improved from a mean of 19.2 prior to treatment to 41.3 after the injection at final follow. Ultrasonography of the involved elbow showed decrease in focal hypoechoic, decreased edema, improvement in thickness of the tendon and healing of the tear at the origin site. This study confirms that local PRP by supplying growth factors helps to enhance the stromal and mesenchymal stem cell proliferation and increases tendon vascularity and prevents angiofibroblastic degeneration and thus improves tendon repair and healing property by releasing growth factors and increasing vascularity, which can be documented by improved tendon morphology.

Keywords: lateral epicondylitis, platelet rich plasma, ultrasonography

Introduction

Lateral epicondylitis is treated non-operatively by rest, anti-inflammatory drugs, brace, physical therapy or by local intralesional injections of corticosteroid, dry needling or by surgical techniques^[1, 2]. But these therapies do not alter the common extensor tendon's poor healing properties secondary to poor vascularization of tendon, which is the basic pathophysiology in tennis elbow^[3]. Hence these traditional therapies have shown inconsistent outcomes.

Recently, platelet rich plasma (PRP) an autologous biological product containing high concentrations of platelet derived growth factors has shown promising results in chronic tendinopathies, when injected locally^[4-7]. Various series and RCTs have shown the efficacy of PRP in treatment of lateral epicondylitis and the advantage of PRP over the corticosteroid injection^[8-22]. But all of these studies have assessed the outcome on a subjective basis only and these series lack objective evidence of the improvement of the healing of the tendon. Ultrasonography of common extensor tendon can be used objectively to document the severity of lateral epicondylitis^[23, 24]. Hence, we tried to measure the efficacy of locally injected autologous PRP for treatment of recalcitrant lateral epicondylitis, functional by Oxford elbow score as well as by ultrasonographic evaluation of the morphologic changes in common extensor origin at the lateral epicondyle before and after the injection, to document outcome objectively.

Material and method

Patients presenting with clinical signs and symptoms of lateral epicondylitis and refractory to the conventional treatment for 3 months, fulfilling the inclusion and exclusion criteria, were treated by local autologous platelet rich plasma (PRP) injection and were included in the study.

The study design was approved by the ethical committee of the institution and written consent was obtained from all the participants.

All patients coming to the OPD with pain and tenderness localized to lateral epicondyle with positive Cozen test, Mills test and/or Maudslay's test along with or without restriction of forearm rotation were diagnosed to be patients of lateral epicondylitis or tennis elbow. These patients were initially given oral anti-inflammatory and analgesic treatment along with elbow brace and physiotherapy in form of exercises, deep tissue massage and ultrasound therapy. Patients not responding even after 3 months of conservative treatment were labelled as the recalcitrant cases and were included in the study. Patients older than 60 years, with bilateral involvement, symptoms of carpal tunnel syndrome or cervical radiculopathy, systemic disorders (diabetes, rheumatoid arthritis, or hepatitis) or who had undergone surgery or local corticosteroid injection in the past 6 months or with local skin disease at elbow were excluded from the study.

Patients in the study were investigated with complete blood count, blood urea, serum uric acid, blood glucose levels, rheumatoid factor, liver function test and ESR. Range of motion was assessed and radiographs of the involved elbow were taken to rule out other elbow pathology.

Ultrasonography of the involved elbow was also done to evaluate tear at the common extensor origin, focal hypoechoic, oedema, cortical erosion, calcification, thickness and fraying of the common extensor tendon and probe induced tenderness and was compared with normal elbow. Pre injection pain score (visual analogue scale) and Oxford elbow score were calculated.

10 ml of autologous blood was collected in an acid citrate dextrose vacutainer and was passed through a two stage centrifuge (first stage at 1600 rpm for 15 minutes for separation of erythrocytes, and the next stage at 2800 rpm for 7 minutes in order to concentrate platelets) to separate the blood into three layers. The lower most layer contain erythrocytes and leukocytes, the middle buffy layer contains most of the platelets with platelet concentration of $1,227,000 \pm 250,000/\mu\text{l}$ (i.e. 4-6 times the average normal values) and the uppermost layer contains mostly plasma. The middle buffy layer of the platelet concentrate was collected in a sterile syringe.

Under all aseptic precautions, 1 ml of PRP was injected at the most tender point over the lateral epicondyle of the humerus by peppering technique. After injection, patients were rested for 30 minutes and were advised against massage or hot fomentation. Ice packs and paracetamol were advised for discomfort rather than non-steroidal anti-inflammatory drugs, as the latter may interfere with platelet function.

Patients were regularly followed at 2 weeks, 6 weeks, 3 months, and 6 months. Post injection patient's outcome was re-assessed using the visual analogue scale (VAS) for pain and Oxford Elbow Score. Ultrasonography of the involved elbow was performed again at final outcome of 6 months by an experienced musculoskeletal sonologist to re-evaluate for tear at the common extensor origin, oedema at the common extensor origin, cortical erosion, probe-induced tenderness, and thickness of the tendon. All the gathered data was tabulated and statistical analysis done.

Result

30 patients with mean age 39.3 years (range 25 to 58) of tennis elbow were included in the study. Out of these 22 (73%) were female and 8 (27%) were male. 24 (80%) of the patients of tennis elbow had complains in right elbow with right to left ratio of 4:1. Most of our patients had right dominance i.e. 23(76%) patients. None of the cases had bilateral involvement. The mean duration of symptoms was 7.2 months (range 5 to 13 months).

The mean pain VAS Score improved from 7.7 before injection to 5.4 after 2 weeks, 4.1 after 6 weeks, 3.2 at 12 weeks of injection and 1.8 at final follow up i.e. after 6 months post injection, respectively. At the initial presentation, out of the 30 patients, 19 patients had severe pain whereas 11 patients had moderate pain before injection, which improved to only 3 patients having moderate pain and none of the patients having severe pain at elbow at final follow up after the injection. 27 patients had either no or mild pain only at the lateral elbow (table 1).

Very severe to severe tenderness at the lateral epicondyle of elbow prior to injection was seen in 28 (93%) patients, which improved to, none of the patients having severe or very severe tenderness and 28 (93%) patients having either no or only mild tenderness at the lateral elbow at final follow-up.

Table 1: Results of the patients of tennis elbow after autologous PRP injection

Parameter	Grading	Pre-injection	Post – injection			
			2 week	6 week	12 week	6 month
Pain (VAS score)	No (0)	0	0	1	2	8
	Mild (1-2)	0	2	11	20	19
	Moderate (3-6)	11	26	18	8	3
	Severe (7-10)	19	2	0	0	0
	Mean VAS score	7.7	5.4	4.1	3.2	1.8
Tenderness	No or mild	0	3	12	25	28
	moderate	2	8	16	4	2
	Severe	22	18	2	1	0
	Very severe	6	1	0	0	0
Oxford elbow score	0-19 (worst)	19	4	1	1	0
	20-29 (severe)	9	15	8	2	1
	30-39 (moderate)	2	10	16	16	6
	40-48 (mild to normal)	0	1	5	11	23
	Mean OES	19.2	28.6	32.4	39.6	41.3
USG of common extensor	Tear	18	-	-	-	7
	Oedema	14	-	-	-	2
	Thinning and fraying	6	-	-	-	2
	Probe induced tenderness	29	-	-	-	6
	Cortical erosion	24	-	-	-	24

	Calcification	4	-	-	-	4
	Focal hypo-echoic	26	-	-	-	6
Range of motion	90 ⁰ -110 ⁰	1	0	0	0	0
	110 ⁰ -130 ⁰	5	2	0	0	0
	130 ⁰ -150 ⁰	24	28	30	30	30

The functional outcome as assessed by the Oxford elbow score improved from a mean of 19.2 prior to treatment to 41.3 after the injection at final follow. Pre injection elbow score was worst to severe in 28 patients, whereas, at final follow up 23 patients had elbow score as normal or mild i.e. between 40 to 48 and 6 patients had oxford elbow score between 30 to 39. Prior to injection 6 patients had restriction in the forearm rotation less than 160 degree. At final follow-up all the patients had normal range of motion.

Prior to injection, ultrasonography of the involved elbow showed tear at the common extensor origin in 18, oedema in 14, cortical erosion in 24, calcification in 4, thinning and

fraying of the common extensor tendon in 6 and probe induced tenderness in 29 patient (fig 1). Focal hypoechoic in the deep part of common extensor tendon was seen in 26 patients before injection, whereas only 6 patients showed these focal hypoechoic in deep common extensor tendon after 6 months of the injection, indicating the evidence of healing in the tendon. At final follow up only 7 patients had ultrasonographic evidence of tear at common extensor origin, oedema in 2 patients, cortical erosion in 24, 2 patients had thinning and fraying of common extensor origin, and probe induced tenderness was seen in only 6 patients (table 1).

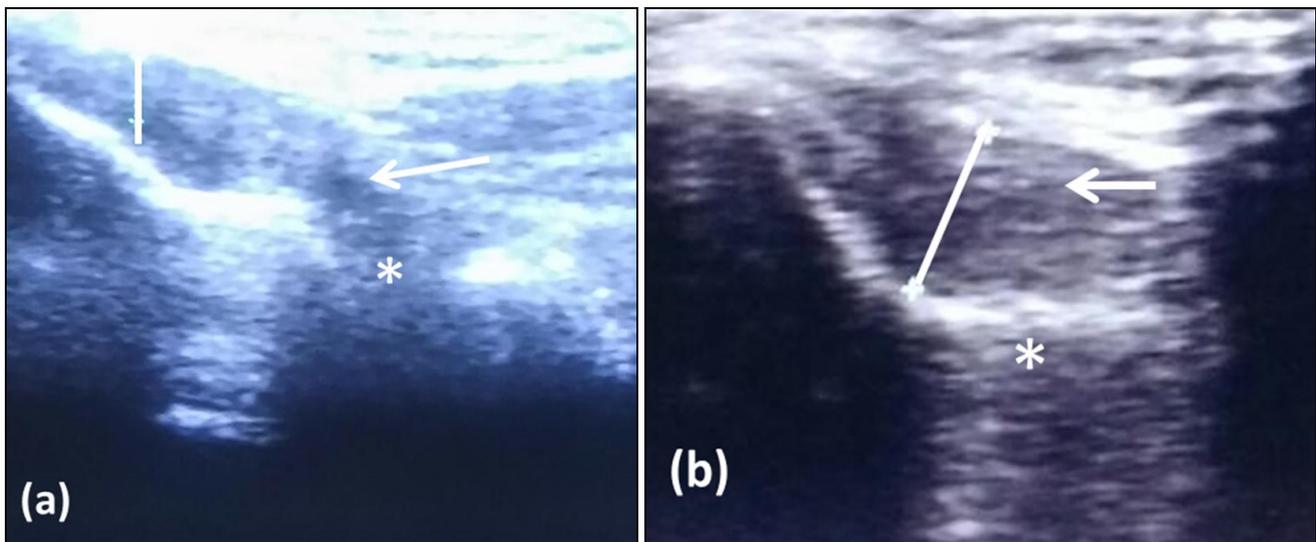


Fig 1(a) and (b): Longitudinal sonogram finding of a 34 years male presenting with tennis elbow (a) pre injection sonography shows focal hypoechoic (white arrow), mild tear at origin (asterix), fraying and thinning (3.1mm - shown as straight line between plus) of the common extensor tendon (b) 6 months post PRP injection shows reduced focal hypoechoic with increased in thickness of tendon (5.6mm) and healing in the tear at the origin

Two patients came up with complaints of post injection pain and swelling at injection site at one week of post injection and one patient came up with fever, both of these complaints were relieved by analgesics and antibiotics medications respectively. None of the patients showed any other complication, like infection, neurovascular change or worsening of epicondylar pain.

Discussion

Lateral elbow epicondylar tendinosis or tennis elbow (TE) is very common condition among persons performing activities involving strong gripping and repetitive wrist extension [1, 2]. Lateral epicondylitis is usually a misnomer because microscopic evaluation of tendon does not show signs of inflammation. It has been well proven by histologically that lateral epicondylitis or tennis elbow is not an acute inflammatory pathology, but instead it is failure of the normal tendon repair mechanism along with angiofibroblastic degeneration because tendons are relatively hypovascular. This hypovascularity may lead to hypoxic tendon degeneration which is main aetiology of tendinosis [3, 24, 25].

The traditional methods of treatment to treat tennis elbow, including rest, anti-inflammatory medications, bracing, physical therapy, iontophoresis, extra corporal shockwave,

botulinum toxin, and corticosteroid injection, do not alter the tendon's poor healing properties secondary to poor vascularization of tendon, which is the basic pathophysiology in tennis elbow [1-3]. Hence these methods have shown inconsistent outcome.

Autologous biological blood-derived product PRP releases high concentrations of platelet derived growth factors on injection which enhance tendon healing due to its effects on angiogenesis and collagen synthesis. Various growth factors and cytokines in PRP include Platelet Derived Growth factors (PDGF-aa, PDGF-bb, PDGF-ab), Vascular Endothelial Growth Factor (VEGF), Fibroblast growth factor (FGF), Epidermal Growth Factor (EGF), Transforming Growth Factor beta (TGF-b1, TGF-b2), Insulin Like Growth Factor-1 and 2 (IGF-1, IGF-2), Interleukin - 8 (IL-8), Keratinocyte Growth Factor, Connective Tissue growth factor. The role of PRP in bone, wound and tendon healing is well established [27-29].

Recent literature is saturated with articles on the efficacy of PRP in treatment of tennis elbow. Various studies by Mishra *et al.*, Hecthman *et al.*, Tan *et al.*, Palacio *et al.* has already confirmed the efficacy of the PRP in treatment of tennis elbow [8-13]. Several studies have even compared the efficacy of PRP with corticosteroid injection or with whole blood injection like Gosen *et al.*, Peerbooms *et al.*, Krogh *et al.*,

Lediedzinski *et al.*, Raeissadat *et al.*, and Thanasas *et al.* [13-22]. All of studies confirmed the efficacy of PRP injection and showed the advantage of PRP over the corticosteroid injection or whole blood.

But all of the studies have measured the results in terms of the pain relief as assessed on the VAS score or as assessed on the improved in functional elbow scores like Mayo, Oxford, Nirschl score etc. But both these parameter pain as well as the functional elbow score are subjective in nature and lack to give objective evidence of healing of the tendon and are thus subject to bias.

Ultrasonography of the tendon enables to visualize the tendon structures around the elbow [23-24]. Thus changes in the USG finding of the common extensor origin before the injection and after the injection can give the documented evidence of the improvement in the pathology of the tendon. Hence we tried to document the efficacy of the local autologous PRP injection in treatment of tennis elbow by pain relief as assessed by VAS score, improvement in functional elbow score as assessed by Oxford elbow score and to objectively document the improvement by seeing the changes in USG findings in the common extensor morphology so that we can get an objective evidence of the healing and improvement.

Our results subjectively as well as objectively confirmed the efficacy of the autologous PRP injection in the treatment of recalcitrant tennis elbow as there is improvement in VAS score, Oxford elbow functional score as well as improvement seen in the sonographic appearance of the morphology of the common extensor tendon origin after the local autologous PRP injection as seen as decrease in focal hypoechoic, decreased edema, improvement in thickness of the tendon and healing of the tear at the origin site. Thus this study confirms that local PRP by supplying growth factors helps to enhance the stromal and mesenchymal stem cell proliferation and prevents fibrous scarring of the tendon. This increase in tendon vascularity by PRP prevents angiofibroblastic degeneration due to hypovascularity of the tendon, which is the main pathophysiology in tennis elbow. This locally injected PRP has led to improved tendon repair and healing property by releasing growth factors and increasing vascularity, which can be documented by improved tendon morphology. This study is limited by lack of randomized group, a relatively smaller sample size and short follow up time.

Conclusion

PRP is an effective mode of treatment of recalcitrant tennis elbow, as it has tendency to enhance the healing potential of the hypovascular tendon by releasing high concentration of growth factors and this improvement has been documented subjectively by improvement in elbow score and objectively by improved tendon morphology on sonography.

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