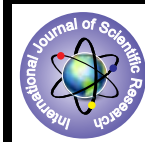


Local Injection of Platelet Rich Plasma Versus Corticosteroids For Treatment of Lateral Epicondylitis of Humerus



Medical Science

KEYWORDS :

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INTRODUCTION:

Lateral epicondylitis, commonly known as Tennis Elbow is one of the most common causes of musculoskeletal pain involving common extensor origin of the forearm. The disorder arises as a result of repetitive strain injury involving overexertion of wrist and finger extensors. It is the most frequent type of myotendinosis at the common extensor tendon origin [1,2]. The frequency of lateral epicondylitis is reported between 1 to 3% among normal nonathlete population [3].

The precise treatment of this condition is yet to be elucidated because the pathophysiology of the disease is not clearly understood. Activities requiring repeated contraction of the wrist extensors are implicated, with the extensor carpi radialis brevis (ECRB) tendon most commonly involved. [9]

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]. Treatment options include rest, non-steroidal anti-inflammatory medication, physical therapy, extracorporeal shock wave therapy, ultrasound therapy, botulinum injection, and corticosteroid (CS) injection, splinting. Recalcitrant cases necessitate surgical release. However, these traditional therapies do not alter the tendon's inherent poor healing properties secondary to poor vascularization [7,8]. Given the inherent nature of the tendon, new treatment options including platelets rich plasma (PRP), autologous blood are aimed at inducing inflammation rather than suppressing it [4,5,6]. Platelet rich plasma is a volume of the plasma fraction of autologous blood having a platelet concentration above baseline, a new treatment regime. Platelets have strong growth factors which play a major role in healing of chronic injuries. Platelet-rich plasma (PRP) enhances healing by delivering high concentrations of alpha-granules containing biologically active moieties (such as vascular endothelial growth factor and transforming growth factor- α) to the areas of soft-tissue damage [12,13]. In PRP, platelet count increases 2- to 8-fold, and different growth factors increase 1- to 25-fold. [14]

Therapeutic PRP should have a platelet concentration 4 to 6 times greater than that of whole blood ($200000/\text{mm}^3$) [6]. The concentrations less than or greater than this amount

may be ineffective or inversely lead to suppression of the healing process [4,5]. Autologous blood is an effective alternative to PRP but the platelet concentration is much lower.

Considering the high cost of autologous PRP therapy, this study was designed to evaluate the efficacy of corticosteroid injection as a less costly treatment versus PRP in patients suffering from chronic lateral epicondylitis.

PATIENTS AND SETTING.

All patients with clinical signs and symptoms of chronic lateral epicondylitis during May 2012 – May 2016 referring to K.E.M. Hospital were evaluated to enter this randomized, single blind study.

INCLUSION CRITERIA

Criteria for inclusion in the study were clinically diagnosed lateral epicondylitis (based on symptoms, site of tenderness, and pain elicited with resisted active extension of the wrist in pronation).

EXCLUSION CRITERIA.

Patients were excluded if they were pregnant, older than 75 years, had history of trauma, platelet dysfunction syndrome, coagulopathies, local infection, any recent febrile or infectious disease, use of corticosteroids during last 2 weeks, a history of local injection of any medications (steroid, whole blood, PRP, or dry needling) into the site of lateral epicondyle, hemoglobin $< 10 \text{ gm/dl}$, plasma platelet count $< 10,0000 / \text{mm}^3$, cervical radiculopathy or peripheral radial nerve injury, systemic illnesses like ischemic heart disease, diabetes, rheumatoid arthritis, hepatitis, any bony malformations, bony or articular lesions at elbow confirmed radiologically.

METHOD:

From the ethical point of view, all patients gave written consent for inclusion in the study. The process of the treatment was explained to the patients, the written consent form was signed or fingerprinted by the patient. Ethical clearance from the ethics committee was obtained before commencement of the study.

Sixty five patients of both genders between 21-60 years of age suffering from lateral epicondylitis were recruited for the study after obtaining written informed consent. Com-

plete physical examination and relevant investigations including complete haemogram, fasting blood sugar (FBS) and plain X-ray of involved elbow were done. Selected patients were randomized to 2 groups (A and B).

Group A patients received a single injection of PRP (1ml), with absolute platelet count of 1 million platelets/ mm³ as confirmed by manual counting. PRP was injected into the common extensor origin

at the lateral epicondyle of the humerus under aseptic conditions.

Group B patients received a single injection of corticosteroid (methylprednisolone, 40mg in 1ml). The site of injection and the technique used was same in both the groups. Patients were followed up at 2 weeks, 4 weeks and 3 months.

For preparing 1 mL of PRP, 10 mL of blood was first collected from the patient's upper limb cubital vein using an 18G needle. Then 1 mL of ACD-A was added to the sample as an anticoagulant. One mL of the blood sample was sent for complete blood count. The rest of the sample passed through two stages of centrifuge (first with 1600 rpm for 15 minutes for separation of erythrocytes and next with 2800 rpm for 7 minutes in order to concentrate platelets). For pain relief only, oral paracetamol and ice therapy were used. Patients of both groups were requested to refrain from heavy labor activities for a week. Three days after the injection, each patient was started on a simple program of extensor muscles stretching and 2 weeks after injection eccentric loading exercises were started. Full activities of daily living were started after 8 weeks.

PARAMETERS :

Pain intensity: This was assessed using the Visual Analog Scale (VAS), a subjective assessment scale of perceived pain. VAS uses a numerical scale ranging from 0 to 10, where 0 indicates no pain and 10 indicates maximum possible pain.

Functional outcome: Functional outcome was measured using quick Disabilities of the Arm, Shoulder and Hand scale (qDASH) before intervention and in all three follow up visits.

Statistical Analysis

Statistical Analysis was done on SPSS for windows version. MannWhitney test and Wilcoxon test was used for non-parametric data while t-test was used for normal distributed data. The results were considered significant at 5% of significance (p-value < 0.05).

Results

Out of the 65 patients recruited for the study, five were lost to follow up. 60 patients completed 3 months follow up, 30 in each group. Group A patients received PRP local injection and Group B patients received methyl-prednisolone local injection. The study could not be completed in 5 patients because of failure of follow up.

	Group A	Group B
Age	38.9	39.1
Duration of symptoms(months)	2.1	2.2

Table 1 depicting demographic characteristics of study population.

Pain- Pain was assessed using the VAS. The VAS score improved more with corticosteroid injection after 15 days (p<0.0001) and at 4 weeks (0.018) however, at the end of three months improvement in pain was significantly better in PRP injection group (p<0.0001).

	0 day	15 days	4 weeks	3 months
Group A	7.8	5.8	4.6	1.7
Group B	7.9	4.9	3.4	2.9
p-value		< 0.0001	< 0.01825	< 0.0001

The table 2 depicting the VAS (Visual analogue scale) score in group A and B

Functional outcome- Functional outcome was measured using q-DASH scale. Improvement of q-DASH score was observed in both the groups. Improvement was statistically significant in the follow up visits in the both the groups. Functional outcome measure (qDASH) showed better improvement (p<0.001) at the end of 3 months in group A. Group B had statistically significant (p<0.05) and better improvement than Group A at 15 days and 1 month follow up period while at 3 month follow up group A had better improvement on each parameter over Group B (p< 0.05).

	0 day	15 days	4 weeks	3 months
Group A	88	76.3	62.4	33.02
Group B	90	70.4	53.05	44.4
p-value		<0.0001	0.009	<0.0001

The table 3 showing qDASH score.

None of the patients reported any adverse affects.

DISCUSSION:

The pathogenesis of tendinopathy is triggered by a high dose cyclic strain that causes oxidative stress and the induction of cartilage genes. These two major pathways lead to apoptosis and a loss of matrix integrity, causing metalloproteinase activity. As a result, a degeneration and regeneration process begins. This process is accompanied by vascular infiltration and nerve regeneration[11]. Edwards and Calandruccio (15) suggested the possible mechanism of action of autologous blood injection to be that chemical modifiers, which are known to be mitomorphogenic and carried in the whole blood, provide the necessary cellular and humoral mediators to induce a healing cascade of degenerated tendinous origin of extensor carpi radialis brevis (15)

In this study we compare the efficacy between local administration of corticosteroids and PRP. CS suppresses the immune system by suppressing the pro-inflammatory proteins. Its potential side effects include lipodystrophy, skin pigmentation changes, and tendon atrophy/ruptures. PRP is an increasingly popular treatment for LE. It increases expression of the collagen gene and production of vascular endothelial growth factor and hepatocyte growth factor in human tenocytes[16,17] and type-I collagen[18]. PRP initially inhibits the inflammatory process and then stimulates proliferation and maturation of the healing process. It enhances stromal and mesenchymal stem cell proliferation[19] and prevents the fibrous scar tissue healing that occurs with macrophage-mediated tendon-to-bone healing[20]. PRP may also suppress macrophage proliferation and interleukin-1 production within the first 72 hours.[21,22]. Increase in tendon vascularity following PRP injection is associated with improved tendon morphology.[23]

Another review performed by Smidt et al. [25] evaluated thirteen randomized controlled studies regarding the use of local corticosteroid injections in tennis elbow and found that local corticosteroid injections have superior benefit (pain, global improvement and grip strength) in the short-term (≤ 6 weeks) compared to placebo, local anesthetic and conservative treatment. However, this benefit was not sustained in the intermediate (6 weeks–6 months) or long-term (≥ 6 months). The mechanism of short-term relief following steroid injection is not clear. It may, however, be attributed to bleeding into the degenerated area through fenestrations by needling. Since corticosteroid injections do not address the pathophysiology of the disease, the results are not sustained in the long-term.

CONCLUSION:

In our study with 60 patients followed up for 3 months with 30 patients in each group the pain scores during first 2 weeks and at 4 weeks were better with corticosteroid injection locally than the PRP administration. Both groups had clinically and statistically significant improvement at 3 months followup. However the long term follow up at 3 months showed that both the pain scores and functional outcomes were better and statistically significant in PRP group than the CS injection group. Hence it is safe to conclude that though the corticosteroids provide short term benefit and relief of pain, PRP administration significantly improves the functional outcomes on the long run, risk free and with less recurrence rates.

REFERENCES:

- M.A. Childress and A. Beutler, "Management of chronic tendon injuries," *American Family Physician*, vol. 87, pp. 486–490, 2013.
- A. O. Chourasia, K. A. Buhr, D. P. Rabago et al., "Relationships between biomechanics, tendon pathology, and function in individuals with lateral epicondylitis," *Journal of Orthopaedic & Sports Physical Therapy*, vol. 43, pp. 368–378, 2013.
- A. Mishra and T. Pavelko, "Treatment of chronic elbow tendinosis with buffered platelet-rich plasma," *American Journal of Sports Medicine*, vol. 34, no. 11, pp. 1774–1778, 2006.
- D. Crane and P. Everts, "Platelet rich plasma (PRP) matrix grafts," *Practical Pain Management*, vol. 8, pp. 11–26, 2008.
- K. Tate and D. Crane, "Platelet rich plasma grafts in musculoskeletal medicine," *The Journal of Prolotherapy*, vol. 2, pp. 371–376, 2010.
- S. Sampson, M. Gerhardt, and B. Mandelbaum, "Platelet rich plasma injection grafts for musculoskeletal injuries: a review," *Ethics in Science and Environmental Politics*, pp. 1–10, 2008.
- M. Kazemi, K. Azma, B. Tavana, F. Rezaiee Moghaddam, and A. Panahi, "Autologous blood versus corticosteroid local injection in the short-term treatment of lateral elbow tendinopathy: a randomized clinical trial of efficacy," *American Journal of Physical Medicine and Rehabilitation*, vol. 89, no. 8, pp. 660–667, 2010.
- T. Molloy, Y. Wang, and G. A. C. Murrell, "The roles of growth factors in tendon and ligament healing," *Sports Medicine*, vol. 33, no. 5, pp. 381–394, 2003.
- Non-surgical treatment of lateral epicondylitis: a systematic review of randomized controlled trials Susan E. G. Sims, Katherine Miller, John C. Elfar, and Warren C. Hammert
- Autologous Blood Injection Works for Recalcitrant Lateral Epicondylitis Bora Bostan,1 Orhan Balta,1 Murat Aşçı,1 Kürşad Aytekin,2 and Enes Eser³
- Xu Y, Murrell GA. The basic science of tendinopathy. *Clin Orthop Relat Res*. 2008;466:1528–38. <http://dx.doi.org/10.1007/s11999-008-0286-4>. [PMC free article] [PubMed]
- Gandhi A, Dumas C, O'Connor JP, Parsons JR, Lin SS. The effects of local platelet-rich plasma delivery on diabetic fracture healing. *Bone* 2006;38:540–6.
- Pietrzak WS, Eppley BL. Platelet rich plasma: biology and new technology. *J Craniofac Surg* 2005;16:1043–54.
- Hall MP, Band PA, Meislin RJ, Jazrawi LM, Cardone DA. Platelet-rich plasma: current concepts and application in sports
- Edwards SG, Calandruccio JH. Autologous blood injection for refractory lateral epicondylitis. *J Hand Surg Am*. 2003;28:272–8. <http://dx.doi.org/10.1053/jhsu.2003.50041>. [PubMed]
- de Mos M, van der Windt AE, Jahr H, van Schie HT, Weinans H, Verhaar JA, et al. Can platelet-rich plasma enhance tendon repair? A cell culture study. *Am J Sports Med* 2008;36:1171–8.
- Kajikawa Y, Morihara T, Sakamoto H, Matsuda K, Oshima Y, Yoshida A, et al. Platelet-rich plasma enhances the initial mobilization of circulation-derived cells for tendon healing. *J Cell Physiol* 2008;215:837–45.
- Lucarelli E, Beccheroni A, Donati D, Sangiorgi L, Cenacchi A, Del Vento AM, et al. Platelet-derived growth factors enhance proliferation of human stromal stem cells. *Biomaterials* 2003;24:3095–100.
- Kawamura S, Ying L, Kim HJ, Dymbil C, Rodeo SA. Macrophages accumulate in the early phase of tendon-bone healing. *J Orthop Res* 2005;23:1425–32.
- Woodall J Jr, Tucci M, Mishra A, Asfour A, Benghuzzi H. Cellular effects of platelet rich plasma: interleukin-1 release from PRP treated macrophages. *Biomed Sci Instrum* 2008;44:489–94.
- Woodall J Jr, Tucci M, Mishra A, Benghuzzi H. Cellular effects of platelet rich plasma: a study on HL-60 macrophage-like cells. *Biomed Sci Instrum* 2007;43:266–71.
- Mishra A, Collado H, Fredericson M. Platelet-rich plasma compared with corticosteroid injection for chronic lateral elbow tendinosis. *PMR* 2009;1:366–70.
- Chaudhury S, de La Lama M, Adler RS, Gulotta LV, Skonieczki B, Chang A, et al. Platelet-rich plasma for the treatment of lateral epicondylitis: sonographic assessment of tendon morphology and vascularity (pilot study). *Skeletal Radiol* 2013;42:91–7.
- Am J Sports Med*. 2006 Nov;34(11):1774-8. Epub 2006 May 30. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. Mishra AI, Pavelko T.
- Smidt N, Assendelft WJ, van der Windt DA, Hay EM, Buchbinder R, Bouter LM. Corticosteroid injections for lateral epicondylitis: a systematic review. *Pain*. 2002;96:23–40. [http://dx.doi.org/10.1016/S0304-3959\(01\)00388-8](http://dx.doi.org/10.1016/S0304-3959(01)00388-8). [PubMed]