# Could Platelet-Rich Plasma Local Injection Be a Good Injectable Alternative Option for The Treatment of Chronic Lateral Epicondylitis in Terms of Safety and Efficacy?

<sup>1</sup> Lec.Dr. Dheyaa Mohammed Abdulwahab, orthopedic surgeon Department of surgery, Iraqia Med school, <u>Diaamalosh@gmail.com</u>

<sup>2</sup>Dr. Saif Mohammed Kani,orthopedic surgeon ,Baghdad medical city,CABOS Saif\_kani@yahoo.com

<sup>3</sup>Ass.Prof. Dr. Waleed faris Abdul qader, orthopedic surgeon Department of surgery, Iraqia Med school, waleedfaris44@gmail.com

<sup>4</sup>Prof. Dr. Younis Abdul Rahman Rasheed Al Radhwany, Orthopedic Surgeon Department of surgery, Iraqia Med school. yyy\_alradwani@yahoo.com

## Abstract

**Background**: Tennis elbow, also known as lateral epicondylitis, refers to a degenerative condition affecting the common origin of the forearm's extensor muscles & is a rather frequent ailment for which individuals seek therapy. It's a condition that significantly limits a person's function and movement, necessitating many visits to orthopedic specialists each year. The main symptoms were continuous discomfort and soreness around the lateral epicondyle, as well as an inability to perform everyday tasks & and it is most prevalent in the fourth and fifth decades of life. Rest, bracing, prescription of nonsteroidal anti-inflammatory medications, physiotherapy, and extracorporeal shock wave therapy are among conservative therapeutic options. Corticosteroid injections and regeneration injections are two more conservative treatment approaches. The injections are used to postpone and/or eliminate the need for surgery. The use of endogenous growth factors in LE therapy has shown encouraging outcomes in vitro and in vivo, because to advances in molecular biology and regenerative medicine. The aim of this study is to evaluate the PRP local injection for the treatment of LE in terms of safety and efficacy.

**Patients and methods:** a prospective design clinical study, 41 patients were enrolled. Chronic clinically confirmed lateral epicondylitis (based on symptoms, location of tenderness, and pain evoked with resisted active extension of the wrist in pronation and elbow extension) with symptoms lasting more than 3 months & pain severity of at least 5 (based on a 10 scale VAS (Visual Analogue Score) was the criterion for inclusion in the research. For PRP preparation, noncommercial kit was used to process the PRP; 20 ml of blood was drawn from the patient's upper leg cubital vein in order to prepare 2 ml of PRP. Injection of PRP whiles the patient in a comfortable and sterile posture that enables for easy access to the injection site. The injection site's skin was prepared and draped, then the liquid PRP was injected in a sterile environment, the patient had a PRP injection at the maximum location at the elbow. A visual analog scale (VAS) was used to measure pain in the patients at baseline, at 3 and 6 months.

**Results**: 41 patients enrolled in this study. After the intervention, all of the patients were followed up with as outpatients at 3 & 6 months. The patients were 41.6+/-6.2 years old on average. There were 29 female patients (70 percent) and 12 male patients (30 percent). Every single one of the patients was right-handed. The average duration of symptoms was 8.1+/-2 months. All patients' average VAS pain levels at baseline were 7.3+/-2.1, whereas mean VAS pain scores at 3 month follow-up were 1.9+/-4.6, and values were dropped to 1.2+/-2.8 at 6 months follow-up. The average VAS score was significantly lowered from baseline at 3& 6 month follow-up, and there was a significant difference between before and after PRP therapy (P >0.01).

**Conclusion**: our trial findings suggest that PRP local injection is a very good option for the treatment of chronic lateral epicondylitis of the elbow in terms of safety and efficacy.

#### Introduction

Tennis elbow, also known as lateral epicondylitis, refers to a degenerative condition affecting the common origin of the forearm's extensor muscles & is a rather frequent ailment for which individuals seek therapy.

It's a condition that significantly limits a person's function and movement, necessitating many visits to orthopedic specialists each year. The incidence of this illness is estimated to be 15.1 cases per 10,000 patients seen [1]. The main symptoms were continuous discomfort and soreness around the lateral epicondyle, as well as an inability to perform everyday tasks & and it is most prevalent in the fourth and fifth decades of life [2,3,4].

Repetitive microtrauma results in tendon degeneration, which causes this disease [5]. The primary contributing causes to repeated microtrauma include overexertion of the extremities with recurrent wrist extension and alternating forearm pronation/supination motions [6]. Traditionally, the issue has been treated conservatively [7], with only a tiny percentage of people opting for surgery to relieve discomfort [8]. Rest, bracing, prescription of nonsteroidal anti-inflammatory medications [9], physiotherapy [10], and extracorporeal shock wave therapy [11] are among conservative therapeutic options. Corticosteroid injections and regeneration injections are two more conservative treatment approaches. The injections are used to postpone and/or eliminate the need for surgery.

Although the diagnosis of lateral tendinosis is simple, most doctors believe the pathogenesis of LE is degenerative, as shown by noninflammatory, persistently degenerative alterations in the extensor carpi radialis brevis muscle origin discovered following surgery [12].Tendonnosis is not an acute inflammatory illness, but rather a failure of the normal tendon healing process linked with angiofibroblastic degeneration, according to histologic findings in chronic patients [13, 14]. Current research has produced a number of biological hypotheses about the cause of tendinosis based on histopathological, biochemical, and clinical findings that show cell apoptosis, angiofibroblastic features, or abnormal biochemical adaptations, implying that the condition is caused by a failed healing response [15].

Corticosteroid injections are a typical conservative non-surgical approach for the treatment of lateral epicondylitis [16]. Injections of corticosteroids suppress immune activity and reduce inflammatory cells and mediators such lymphocytes, macrophages, and mast cells [17]. Corticosteroid injections are used to treat pain induced by inflammation and may be given intra-articularly or extra-articularly. Corticosteroid injections, on the other hand, promote protein catabolism while decreasing type I collagen and glycosaminoglycan synthesis, slowing the healing process [17]. The efficacy of these injections for long-term symptom relief in chronic tendinosis has been questioned at places such as the Achilles tendon [18] because to the absence of inflammation in instances of tendinosis and the restriction of collagen repair by corticosteroids.

The use of endogenous growth factors in LE therapy has shown encouraging outcomes in vitro and in vivo, because to advances in molecular biology and regenerative medicine. Several research have looked at the effects of growth factors, with results indicating that they may help with cellular remodeling and healing time [19].In sports medicine, plasma high in growth factors has been shown to be safe and beneficial in treating tendinopathy such Achilles tendinopathy, patellar tendinopathy, and rotator cuff injuries. They've been proven to cause reparative cells to migrate to an injection site, reverse enthesiopathy's pathological alterations, restore normal structure, ease symptoms, and prevent recurrence [20, 21].

Corticosteroid injection produces greater short-term advantages, according to systematic review data [22, 23], but newer trials imply inferior clinical results in the long run [24, 25]. One component of this inferior result is the much higher recurrence rates observed after corticosteroid injection (72 percent) as compared to physiotherapy (8 percent) and waiting and seeing (10 percent) [10]. Both patients and physicians are concerned about these late negative consequences.

As a result, in our study we evaluate the possible benefits of PRP used in LE in terms of safety and effectiveness as an alternating option to local corticosteroid injections.

## **Patients and methods**

This study was a prospective design clinical study, 41 patients were enrolled. Patients with signs and symptoms of chronic lateral epicondylitis who came to our institution between March 2019 and July 2021 were examined to participate in this research. Chronic clinically confirmed lateral epicondylitis (based on symptoms, location of tenderness, and pain evoked with resisted active extension of the wrist in pronation and elbow extension) with symptoms lasting more than 3 months & pain severity of at least 5 (based on a 10

scale VAS (Visual Analogue Score) [26] was the criterion for inclusion in the research. From an ethical standpoint, we obtained written consent from all patients before enrolling them in the trial.

For PRP preparation, noncommercial kit was used to process the PRP; 20 ml of blood was drawn from the patient's upper leg cubital vein using an 18 G needle in order to prepare 2 ml of PRP with a concentration of 4-6 times the typical normal values. The sample was then anticoagulated with 2 ml of ACD-A. A full blood count was performed on one milliliter of blood. The remainder of the material was centrifuged with 3000 rpm for 15 minutes for separation of erythrocytes and to concentrate platelets). The end result was 2 mL of PRP with leukocytes (leukocyte rich PRP). For the activation of platelets, we did not employ any exogenous factors.

Injection of PRP: The patient is put in a comfortable and sterile posture that enables for easy access to the injection site.

The injection site's skin was prepared and draped, then the liquid PRP was injected using an 18 G needle in a sterile environment, the patient had a PRP injection at the maximum location at the elbow, utilizing a peppering approach that spread in a clock-like fashion.

A visual analog scale (VAS) was used to measure pain in the patients at baseline, at 3 and 6 months.

#### Results

41 patients enrolled in this study. After the intervention, all of the patients were followed up with as outpatients at 3 & 6 months. The patients were 41.6+/-6.2 years old on average. There were 29 female patients (70 percent) and 12 male patients (30 percent). Every single one of the patients was right-handed. The average duration of symptoms was 8.1+/-2 months. Figure 1 shows the patients' characteristics at the start of the trial.



## Fig. 1 shows patients characteristics at the start of the trial

All patients' average VAS pain levels at baseline were 7.3+\- 2.1, whereas mean VAS pain scores at 3 month follow-up were 1.9+\- 4.6, and values were dropped to 1.2+\- 2.8 at 6 months follow-up (Fig. 2). The average VAS score was significantly lowered from baseline at 3& 6 month follow-up, and there was a significant difference between before and after PRP therapy (P <0.01). There were no adverse events recorded throughout the trail or at the 6-month follow-up. There were no infection occurred.



Figure 2: shows changes in VAS score at baseline & at 3 & 6 months

#### Discussion

Tennis elbow is one of the musculoskeletal system's most confusing illnesses& patient who has been on conservative therapy for six months and is still experiencing symptoms is difficult to manage, and surgical care, such as minimally invasive surgery or arthroscopic surgery, is frequently required. It has been shown that lateral epicondylitis is predominantly a condition associated to degeneration in the tendon of common extensor origin (usually extensor carpi radialis brevis), rather than an inflammatory process as was previously thought [27]. Maffuli et al.[28] recognized that tendinopathy is a clinical diagnosis, while tendinitis and tendinosis should only be used after a histological study. With or without therapy, a high number of patients (70-80 percent) report symptom remission within a year [29]. Conservative approach, which includes activity restriction, rest, RICE (Rest, Ice, Compression, and Elevation) therapy, and nonsteroidal anti-inflammatory medicines, is typically the first line of treatment. Manipulation under anesthesia has been shown to have positive outcomes [30]. When NSAIDs and activity moderation fail, a local corticosteroid injection is one of the most often suggested treatments. However, Bisset et al. [31] reported that corticosteroids, although helpful in the short term, had inferior long-term benefits (1 year) than physiotherapy in a randomised control study.

Several researches have looked at the function of platelets in releasing substances that might help and speed up the healing process. According to Edwards [32], the underlying pathophysiology of LE is degenerative tendinosis, not inflammatory tendinitis, and anti-inflammatory medicines should be substituted with a more biological approach to tissue repair and this why we preview its safety and efficacy as an alternative option for local corticosteroid injections.

In 140 patients with persistent elbow tendinosis, Mishra and Pavelko [33] conducted a cohort study comparing local injection of buffered PRP with bupivacaine. The findings indicated that 8 weeks following treatment, the PRP group had a 60 percent improvement in their VAS ratings compared to 16 percent improvement in the control group. When compared to before the treatment, the PRP group reported a 93 percent reduction in pain at the final follow-up which looks similar to our research trail. Similarly, Edwards et al. [34] reported remarkable improvement in symptoms in 28 tennis elbow patients following autologous blood injection. They theorized that autologous blood triggered an inflammatory response, allowing healing to take place in an otherwise degenerative process. As with our research, despite the lack of a control group in this trial, the authors expected that a blood injection would give extra advantages above a saline or steroid injection. They came to this conclusion after seeing how blood injections helped patients who had failed repeated steroid injection attempts while using comparable injection procedures and volumes.

On the other hand, we should mention that some researches demonstrated no substantial reduction in pain ratings following PRP injection, contrary to the findings of our study and the studies cited above and this was found in less than 5%(2 patients) in our research whom had modest response to PRP injection. Shiple BJ performed a research to examine the efficiency of a single platelet-rich plasma (PRP), glucocorticoid (GC), or saline injection in relieving pain in lateral epicondylitis. The major outcome measure was the pain intensity scale of the Patient-Rated Tennis Elbow Evaluation (PRTEE) questionnaire (least to greatest pain = 0-50 points) [35].

In 2013, Krogh and colleagues randomly assigned 60 people to one of three groups: PRP, corticosteroid, or saline injection. Tennis elbow had been present for at least three months in all of the subjects. They discovered no significant differences in pain or functional improvement across the groups after three months. One cause for the absence of favorable benefits from PRP injection might be a lack of adequate platelets in PRP derivatives in the trials listed above or various techniques of PRP production [36]. However Cell proliferation and total collagen synthesis are stimulated by both platelet-rich and platelet-poor plasma [37,38]. Human tendons treated with PRP have been proven to produce more endogenous growth factors [39,40]. The method outlined above explains why PRP or whole blood treatment may have a long-term impact on healing [41,42].

Finally, our research has several limitations including the absence of a control group and small number of patients. Longitudinal and randomized controlled trials should be conducted to determine sustained effectiveness.

### **Conclusions & recommendations**

Our findings suggest that PRP local injections may consider a very good injectable option in the treatment of LE in terms of safety and efficacy. The absence of a control group, lack of objective evaluations, limited sample size, and short-term outcomes are all limitations of this exploratory study, and to get a better picture, a bigger, multicenter, randomized controlled experiment is needed.

#### References

- 1. Degen RM, Conti MS, Camp CL, Altchek DW, Dines JS, Werner BC. Epidemiology and disease burden of lateral Epicondylitis in the USA: analysis of 85,318 patients. HSS J. 2018;14:9–14
- 2. Gliedt JA, Daniels CJ. Chiropractic treatment of lateral epicondylitis: a case report utilizing active release techniques. J Chiropractic Med. 2014;13(2):104–9.
- 3. Serafini G. Treatment of lateral epicondylitis. Ultrasound Guid Musculoskeletal Proced. 2012;45(4):340-3
- 4. Ruch DS, Orr SB, Richard MJ, Leversedge FJ, Mithani SK, Laino DK. A comparison of debridement with and without anconeus muscle flap for treatment of refractory lateral epicondylitis. J Shoulder Elb Surg. 2015;24:236–41
- 5. Degen RM, Cancienne JM, Camp CL, Altchek DW, Dines JS, Werner BC. Three or more preoperative injections is the most significant risk factor for revision surgery after operative treatment of lateral epicondylitis: an analysis of 3863 patients. J Shoulder Elb Surg. 2017;26:704–9.
- 6. Goldie I. Epicondylitis lateralis humeri (epicondylalgia or tennis elbow). A pathogenetical study. Acta Chir Scand Suppl. 1964;57:331–9.
- 7. Sanders TL, Maradit Kremers H, Bryan AJ, Ransom JE, Morrey BF. Health care utilization and direct medical costs of tennis elbow: a population-based study. Sports Health. 2016;8(4):355–8.
- 8. Calfee RP, Patel A, DaSilva MF, Akelman E. Management of lateral epicondylitis: current concepts. J Am Acad Orthop Surg. 2008;16(1):19–29
- 9. Jeon JY, Lee MH, Jeon I-H, Chung HW, Lee SH, Shin MJ. Lateral epicondylitis: associations of MR imaging and clinical assessments with treatment options in patients receiving conservative and arthroscopic managements. Eur Radiol. 2018;28(3):972–81.
- 10. Stasinopoulos D, Stasinopoulos I. Comparison of effects of eccentric training, eccentric-concentric training, and eccentric-concentric training combined with isometric contraction in the treatment of lateral elbow tendinopathy. J Hand Ther. 2017;30:13–9.
- 11. Altun RD, Incel NA, Cimen OB, Sahin G. Efficacy of ESWT for lateral Epicondylitis treatment: comparison with physical therapy modalities. J Musculoskelet Res. 2018;21:1850001. https://doi.org/10.1142/S021895771850001X.

- 12. Omar AS, Ibrahim ME, Ahmed AS, Said M. Local injection of autologous platelet rich plasma and corticosteroid in treatment of lateral epicondylitis and plantar fasciitis: randomized clinical trial. Egypt Rheumatol. 2012;34:43–9.
- 13. Smith MA, Smith WT: Emerging techniques in orthopaedics: platelet-rich plasma. Orthop Nurs. 2011, 30: 260-263. 10.1097/NOR.0b013e3182247c42.
- 14. Sampson S, Gerhardt M: Platelet rich plasma injection grafts for musculoskeletal injuries: a review. Curr Rev Musculoskeletal Med. 2008, 1: 165-174. 10.1007/s12178-008-9032-5.
- 15. Martin J, Merino J, Atilano L, Areizaga LM, Gomez-Fernandez MG, Burgos-Alonso N, Andia I: Platelet-rich plasma (PRP) in chronic epicondylitis: study protocol for a randomized controlled trial. Trials. 2013, 14: 410-10.1186/1745-6215-14-410.
- 16. Sirico F, Ricca F, Nurzynska D, Castaldo C, Spera R, Montagnani S. Local corticosteroid versus autologous blood injections in lateral epicondylitis: meta-analysis of randomized controlled trials. Eur J Phys Rehabil Med. 2017;53:483–91.
- 17. MacMahon PJ, Eustace SJ, Kavanagh EC. Injectable corticosteroid and local anesthetic preparations: a review for radiologists. Radiology. 2009;252:647–61.
- 18. Fredberg U, Bolvig L, Pfeiffer-Jensen M, Clemmensen D, Jakobsen B, Stengaard-Pedersen K. Ultrasonography as a tool for diagnosis, guidance of local steroid injection and, together with pressure algometry, monitoring of the treatment of athletes with chronic jumper's knee and Achilles tendinitis: a randomized, double-blind, placebo-controlled study. Scand J Rheumatol. 2004;33:94–101.
- 19. Gregor S, Paul S, Martin W. Do blood growth factors offer additional benefit in refractory lateral epicondylitis? A prospective, randomized pilot trial of dry needling as a stand-alone procedure versus dry needling and autologous conditioned plasma. Skeletal Radiol. 2013;42(11):1515–20.
- 20. Lhee SH, Park JY. Prospective randomized clinical study for the treatment of lateral epicondylitis: comparison among PRP (platelet-rich plasm), prolotherapy, physiotherapy and ESWT. J Shoulder Elb Surg. 2013;22(10):e30–1.
- 21. Scholten PM, Massimi S, Dahmen N, Diamond J, Wyss J. Successful treatment of athletic pubalgia in a lacrosse player with ultrasound-guided needle tenotomy and platelet rich plasma injection: a case report. Pm & R. 2014;7:79–83.
- 22. Smidt N, Assendelft WJ, Windt van der DA, Hay EM, Buchbinder R, Bouter LM: Corticosteroid injections for lateral epicondylitis: a systematic review. Pain. 2002, 96 (1–2): 23-40. 10.1016/S0304-3959(01)00388-8.
- 23. Gaujoux-Viala C, Dougados M, Gossec L: Efficacy and safety of steroid injections for shoulder and elbow tendonitis: A meta-analysis of randomized controlled trials. Ann Rheum Dis. 2008
- 24. Bisset L, Beller E, Jull G, Brooks P, Darnell R, Vicenzino B: Mobilisation with movement and exercise, corticosteroid injection, or wait and see for tennis elbow: randomised trial. BMJ. 2006, 333 (7575): 939-10.1136/bmj.38961.584653.AE.
- 25. Bisset L, Smidt N, Windt Van der DA, Bouter LM, Jull G, Brooks P, Vicenzino B: Conservative treatments for tennis elbow do subgroups of patients respond differently?. Rheumatology (Oxford). 2007, 46 (10): 1601-1605. 10.1093/rheumatology/kem192.
- 26. Boonstra AM, Schiphorst Preuper HR, Reneman MF, Posthumus JB, Stewart RE: Int Reliability and validity of the visual analogue scale for disability in patients with chronic musculoskeletal pain. J Rehabil Res Dev. 2008, 31: 165-169. 10.1097/MRR.0b013e3282fc0f93
- 27. Nirschl RP: Tennis elbow tendinosis: pathoanatomy, nonsurgical and surgical management. Repetitive motion disorders of the upper extremity. Edited by: Gordon SL, Blair SJ, Fine LJ. 1995, Rosemont, IL: American Academy of Orthopaedic Surgeons, 467-479.
- 28. Maffulli N, Wong J, Almekinders LC: Types and epidemiology of tendinopathy. Clin Sports Med. 2003, 22: 675-692. 10.1016/S0278-5919(03)00004-8.
- 29. Tonks JH, Pai SK, Murali SR: Steroid injection therapy is the best conservative treatment for lateral epicondylitis: a prospective randomised controlled trial. Int J Clin Pract. 2007, 61: 240-246.
- 30. Wadsworth TG: Lateral epicondylitis (tennis elbow). Lancet. 1972, 1: 959-960

- 31. Bisset L, Beller E, Jull G: Mobilisation with movement and exercise, corticosteroid injection, or wait and see for tennis elbow: randomised trial. BMJ. 2006, 333: 939-944. 10.1136/bmj.38961.584653.AE.
- 32. Edwards SG, Calandruccio JH. Autologous blood injections for refractory lateral epicondylitis. J Hand Surg. 2003;28(28):272-8.
- 33. Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. Am J Sports Med. 2006;34(11):1774–8.
- 34. Edwards SG, Calandruccio JH: Autologous blood injections for refractory lateral epicondylitis. The Journal of Hand Surgery. 2003, 28A: 272-278.
- 35. Shiple BJ: How effective are injection treatments for lateral epicondylitis?. Clin J Sport Med. 2013, 23: 502-503. 10.1097/JSM.0000000000042.
- 36. Krogh TP, Bartels EM, Ellingsen T, Stengaard-Pedersen K, Buchbinder R, Fredberg U, Bliddal H, Christensen R: Comparative effectiveness of injection therapies in lateral epicondylitis: a systematic review and network meta-analysis of randomized controlled trials. Am J Sports Med. 2013, 41: 1435-1446. 10.1177/0363546512458237.
- 37. Monto RR: Platelet rich plasma treatment for chronic Achilles tendinosis. Foot Ankle Int. 2012, 33: 379-385. 10.3113/FAI.2012.0379.
- 38. Raeissadat SA, Rayegani SM, Babaee M, Ghorbani E: The effect of platelet-rich plasma on pain, function, and quality of life of patients with knee osteoarthritis. Pain Res Treat. 2013, 2013: 165967.
- 39. Peerbooms JC, Sluimer J, Bruijn DJ, Gosens T: Positive effects of an autologous platelet concentrate in lateral epicondylitis in a double-blind randomized controlled trial: platelet-rich plasma versus corticosteroid injection with a 1-year follow-up. Am J Sports Med. 2010, 38: 255-262. 10.1177/0363546509355445.
- 40. Soee AB, Thomsen LL, Tornoe B, Skov L: Reliability of four experimental mechanical pain tests in children. J Pain Res. 2013, 6: 103-110.
- 41. Taylor DW, Petrera M, Hendry M, Theodoropoulos JS: A systematic review of the use of plateletrich plasma in sports medicine as a new treatment for tendon and ligament injuries. Clin J Sport Med. 2011, 21: 344-352. 10.1097/JSM.0b013e31821d0f65.
- 42. Krogh TP, Bartels EM, Ellingsen T, Stengaard-Pedersen K, Buchbinder R, Fredberg U, Bliddal H, Christensen R: Comparative effectiveness of injection therapies in lateral epicondylitis: a systematic review and network meta-analysis of randomized controlled trials. Am J Sports Med. 2013, 41: 1435-1446. 10.1177/0363546512458237