

A Comparative Study of Platelet-Rich Plasma, Steroid Injection and Normal Saline as Placebo for the Treatment of Lateral Epicondylitis

Hilal Ah Kotwal¹, Raja Rameez Farooqi², Mir Samiullah³

Postgraduate Department of Orthopaedics Govt. Medical College Srinagar J&K, India

Abstract: Background: Lateral elbow pain is common with a population prevalence of 1%–3% and is seen more commonly in non-athletes than athletes. Non-operative methods are the mainstay of treatment being effective in more than 95% of cases. However, there has been much debate about the best treatment modality for this condition. Platelet rich plasma (PRP) has shown promising results in many studies as compared to steroid injection & other modes of conservative management. The study was a comparative trial to validate the short term efficacy of single injection of platelet-rich plasma (PRP), 40mg methyl prednisolone (Depomedrol) and normal saline for lateral epicondylitis. Materials and Methods: In this study, 90 patients with unilateral lateral epicondylitis were randomized into three groups, the PRP group(n=30), the Steroid group(n=30) and Placebo group(n=30) by selecting a sealed envelope. Patients were evaluated at weeks 2, 6, 12, 24 and 36 with visual analog scale (VAS) and facial pain scale (FPS). Patients suffering from elbow pain due to other problems or those who have previously received any form of injection were excluded from the study. Kruskal–Wallis test was used for statistical analyses of FPS at all follow ups. Results: Overall, 58 females and 32 males were included with 30 elbows in each group. the PRP group had equivocal relief compared to Depomedrol group at initial 2 and 6 week follow up and was better in both groups than saline group at these early follow ups. At 12, 24 and 36 weeks the PRP group better pain relief than 40 mg depomedrol ($P < 0.05$) group which in turn had had only moderate benefit compared to the saline injection ($P > 0.05$). Conclusion: Over a short term period, PRP gives better pain relief than 40 mg depomedrol or normal saline in tennis elbow. Pain reduction benefit associated with steroid injection fades by the 24th week of follow-up but lasts longer with PRP injection.

Keywords: Lateral epicondylitis, platelet-rich plasma, tennis elbow, depomedrol, normal saline

1. Introduction

Lateral epicondylitis is also known as tennis refers to pain and tenderness over the lateral epicondyle of the humerus; the pain is exaggerated by resisted dorsiflexion of the wrist or the middle finger. This is a common condition with a population prevalence of 1%–3%^[1]. The peak incidence occurs at around 35–55 years of age.^[2,3] In the UK and Netherlands, the annual incidence of lateral elbow pain in general practice is 4-7/1000 population.^[3,4,5] The term was coined in 1883 as “Lawn-tennis elbow.”^[6] Inflammatory cells are not found in the tendon tissues; therefore, Nirschl *et al.* coined the term “Angiofibroblastic tendinosis” to describe this condition.^[7, 8, 9] It is believed that the injury involves tears (either microscopic or macroscopic) in the origin of the extensor muscles of the wrist especially ECRB, which leads to an inflammatory response and in the chronic cases granulation and fibrous.^[10] Acute onset of symptoms occurs more often in young athletes; chronic, recalcitrant symptoms typically occur in older patients. There is much debate about the best treatment approaches for lateral epicondylitis. Non-operative methods are the mainstay of treatment being effective in more than 95% of cases. Those who fail to respond to conservative therapy may be considered for surgical treatment.^[11]

The goals of nonoperative treatment are to revitalize the unhealthy pain producing tendinosis tissue and includes rehabilitative exercise progression,^[10] corticosteroid injection,^[12] autologous blood injection,^[13] extracorporeal shock wave therapy,^[14] botulinum toxin injection,^[15] and hyaluronic acid with chondroitin sulfate injection.^[16] Platelets in PRP contain growth factors and build up

reparative processes. The action of PRP therapy in chronic tendinopathies is varied and hypothesized to include angiogenesis, increase in growth factor expression and cell proliferation, increase the recruitment of repair cells and tensile strength. Lateral epicondylitis may be characterized by complex changes in the tendon in addition to an inflammatory process. Therefore, PRP owing to its high content of various growth factors is more efficacious as a healing agent.^[17] Single or multiple injections of platelet-rich plasma (PRP) have been shown to be of significance in the management of tennis elbow. Randomized controlled trial comparing efficacy of PRP with other modalities will validate the usefulness of PRP in lateral epicondylitis.^[18] In order to address treatment concerns for patients with lateral epicondylitis; we did a randomized clinical trial to test the effectiveness of steroid injection versus PRP injection versus placebo in treating patients with lateral epicondylitis.

2. Materials and Methods

A total of 90 patients with lateral epicondylitis who presented to us at Bone and Joint Hospital Srinagar Kashmir, between April 2015 and May 2016 were enrolled in this randomized controlled comparative study. The ethics committee of our institution approved this study. All of the included patients were informed regarding their condition. Likewise, the purpose of the study was explained to them, and all agreed to participate by signing an informed consent form. Patients in the age group of 18–50 years of either sex who had unilateral symptoms for more than 6 weeks and not received any injection prior to enrolment were included in the study. Despite the conservative treatment, all patients had inadequate pain relief or functional outcome and were

still experiencing severe pain or limitation of activity. Diagnosis was mainly on clinical grounds i.e. on palpation there was mild to severe tenderness on lateral epicondyle and confirmed by ultrasonographic examination of the elbow. The findings involve hypoechoic signal from the extensor tendons especially ECRB suggestive of edema of the extensor tendon in all cases. Radiographs were examined to rule out other elbow pathologies. Patients excluded from this study were those with history of acute elbow trauma, bilateral cases, elbow arthritis, patients requiring antiplatelet medication for the treatment of ischaemic heart disease, cerebrovascular accidents or other medical conditions, any previous elbow surgeries, other causes of elbow pain such as osteochondritis dissecans of capitellum, posterior interosseous nerve syndrome, cervical disc syndrome, synovitis of radiohumeral joint, cervical radiculopathy, fibromyalgia. A total of 90 patients who met the inclusion criteria were randomized into three groups using sealed envelope method and received either of autologous PRP or depomedrol 40mg or 1 cc normal saline injection at the maximum tender spot in fanlike fashion. The skin was painted with povidone-iodine and ethyl alcohol. One milliliter of 2% lignocaine with adrenaline was injected at the injection site after giving test dose. After 10 min, the proposed injection was injected. The injection was given on and around the tendon and not inside the tendon. After giving injection, patients were given analgesics for the initial two days for pain relief in all the three groups. Patients were advised for rest during initial 2 weeks in the form of refraining from strenuous activities by the extremity under study after the injection.

The patients were evaluated at the baseline and before administration of treatment and at follow up of 2 weeks, 6 weeks, 12 weeks, 24 weeks and 36 weeks. The results were recorded by visual analog scale (VAS) score and facial pain scale (FPS).. The results of FPS were analyzed using nonparametric Kruskal–Wallis test.

3. Results

90 patients including 58 females and 32 males in the age group of 18–50 years were included in the study. The study had thirty elbows in each group. The overall mean ages of the patients in the three groups (PRP, Steroid and Saline) are 35.43 ± 7.53 , 34.82 ± 6.79 and 36.12 ± 6.93 years respectively [TABLE 1]. Female preponderance was observed in all the groups and constituted 64.44% of all patients. Right side was involved in 64 (71%) cases. None of our patients was left hand dominant. All of our patients had duration of symptoms more than 6 weeks (range, 6.5 to 12 weeks) The mean VAS and FPS score pre-treatment in all the groups was not statistically significant and the scores at the end of 12 weeks and 24 weeks treatment showed that PRP and steroid was better than normal saline in control of

pain [TABLE 2]. The benefit associated with steroid injection faded away by 36 weeks and was only moderately better than saline group.

FPS was calculated using appropriate proforma using FPS diagram chart. Kruskal–Wallis test was used to compare the result of FPS among all the three groups as shown in [Table 3]. At all times follow ups, the VAS score improvement in PRP and steroid groups was better than saline group and the difference was statistically significant. At 2, 6 and 12 weeks follow up there was improvement in VAS score of PRP and Steroid group but the difference was statistically insignificant. At 12-week follow up, the VAS score mean ranks in PRP group and depomedrol group improved by 40% and 32%, respectively. The improvement in mean VAS score of PRP group at 24-week and 36 week follow up was better than the steroid group and the difference was statistically significant. The VAS score mean ranks in PRP group and depomedrol group improved by 54% and 7%, respectively at the final follow up. The normal saline group showed worsening of results in VAS score at 24 weeks and 36 weeks.

When we compared FPS scores between PRP and Steroid, The mean ranks of FPS scores in PRP group showed 4% improvement at 12 weeks, and 28% improvement at 24 weeks. The differences in result were not significant at 12 weeks, but significant at 24 weeks, ($P < 0.001$).

Similarly, when we compared FPS scores between PRP and placebo we found that the mean ranks of FPS scores in PRP group showed 47.19% improvement at 12 weeks, and 46.86% improvement at 24 weeks. However, the mean ranks of FPS scores in normal saline group showed worsening at 12 weeks and at 24 weeks. The differences in result were significant ($P < 0.001$) at both 12 weeks and 24 weeks for FPS scores. No complications were found in the group receiving PRP and placebo. However, out of thirty elbows given depomedrol hypopigmentation at the injection site was found in 5 patients with associated subdermal atrophy in 1 patient. No infection was there in any of the patients.

Table 1:

	PRP	Steroid	Saline	P value
AGE(In Years)	35.43 ± 7.53	34.82 ± 6.79	36.12 ± 6.93	NS
Female/ Male	20/10	17/13	21/09	NS
Right/Left	22/8	24/06	18/12	NS
Mean duration of symptoms(in weeks)	9.68	8.36	9.48	NS
Mean VAS Score	6.94	6.92	6.44	NS
Mean Nirschl Stage	4.82	5.22	4.98	NS

Table 2

	PRP	improvement	Steroid	improvement	Saline	improvement
0 weeks	6.94		6.92		6.44	
2 weeks	5.16	26%	4.48	35%	5.84	09%
6 weeks	4.64	33%	4.10	41%	5.78	10%
12 weeks	4.16	40%	4.68	32%	5.72	11%
24 weeks	3.32	52%	5.48	21%	5.98	7%
36 weeks	3.16	54%	6.42	7%	6.32	1%

Table 3: Kruskal-Wallis test to compare the result of FPS score among all the three groups

	PRP	Steroid	Normal Saline
0 weeks	45.82	45.15	45.53
2 weeks	34.43	38.22	42.45
6 weeks	28.87	34.98	40.34
12 weeks	24.23	34.54	42.77
24 weeks	20.77	36.09	44.22
36 weeks	18.45	37.23	46.43

4. Discussion

LE is the most common cause of lateral elbow pain in adults that is encountered in day-to-day practice by most orthopedic surgeons. Although it is typically a self-limiting process, there are many nonsurgical and surgical treatment options available if LE becomes chronic and continues to cause pain.[9] With evolution of various nonsurgical options available for treatment of tennis elbow, PRP injection has been shown to be a promising option in various multicenter studies. However, there are conflicting reports that state that PRP might not be as effective as predicted.

Krogh *et al.* in their study concluded that at 3-month followup, there was no significant reduction in pain in any of the three groups. A greater decrease in tendon thickness was seen in the glucocorticoid group. The glucocorticoid group also showed a greater decrease in Doppler activity. The injection of PRP was the most painful.[19] However, Brkljac *et al.* in their study concluded that an injection of PRP improves pain and function in patients suffering from LE where conservative management has failed.[20] Similarly, Raeissadat *et al.* in their study found that PRP and autologous whole blood injections are both effective methods to treat chronic LE and their efficacy persisted during long term followup. PRP was not superior to AWB in long term followup.[21] Peerbooms *et al.* in their study after 1-year followup found that treatment of patients with chronic LE with PRP reduces pain and significantly increases function, exceeding the effect of corticosteroid injection.[22] Gosens *et al.* in their study concluded that treatment of patients with chronic LE with PRP reduces pain and increases function significantly, exceeding the effect of corticosteroid injection even after a follow up of 2 years. There were no complications related to the use of PRP.[23] Arirachakaran *et al.* in their study concluded that PRP injection can improve pain and lower the risk of complications, whereas autologous blood injection can improve pain, disabilities scores, and pressure pain threshold but has a higher risk of complications.[24]

In our study, we found that at 12-week followup, the pain relief was better in both PRP and corticosteroid injection groups as compared with the normal saline group, but at 24-week follow up, the pain relief was maintained better with PRP than corticosteroid. Patients who had received steroid were asymptomatic at 3-month followup, but at 6-month followup, 33.33% patients complained of a recurrence of pain symptoms that was more than 50% of the initial VAS and FPS score. In PRP group, only 13.33% of patients were symptomatic with VAS score and FPS score more than 50% of the initial value. The difference between PRP and corticosteroid injections was statistically significant.

Krogh *et al.* in their study concluded that the injection of PRP was the most painful. Mishra and Pavelko in their study concluded that treatment of patients with chronic elbow tendinosis with buffered PRP reduced pain significantly. They initially injected bupivacaine with epinephrine into the skin and subcutaneous tissue as a local field block and then 0.5 mL directly into the area of maximum tenderness. Then, 2–3 mL PRP was injected using a 22-gauge needle into the common extensor tendon using a peppering technique. This technique involved a single skin portal and then five penetrations of the tendon.[25]

In our study, we used 2% Xylocaine local infiltration before injection in all three groups and injection was given at the common extensor tendon using peppering technique. Injections were given carefully to avoid directly injecting into the tendon. None of the patient reported pain after PRP injection in our study.

Gautam *et al.* concluded that PRP appeared to enable biological healing of the lesion, whereas corticosteroid appeared to provide short term, symptomatic relief but resulted in tendon degeneration.[26] Park *et al.* in their study concluded that 1.3%–4% people develop hypopigmentation which develops over the initial 1–4 months after the injection and resolves spontaneously over 6–30 months. It can be prevented if intradermal and subcutaneous injections are avoided. Subcutaneous fat atrophy is known to last for 6–12 months after corticosteroid injection, and it is known to be reversible and resolved within 1 year.[27] Our study found that 13 patients out of the thirty patients who received corticosteroid suffered from hypopigmentation at injection site, and three patients suffered from subdermal atrophy. The limitation of the study is that sample size needed for the study was not calculated.

5. Conclusion

Lateral epicondylitis or tennis elbow is a painful debilitating condition of elbow, which creates disturbance in functional activities. A single injection of PRP at the site of the elbow pain resulted in relief of pain in patients with longer duration as compared to local steroids to other conservative treatments. However, still more studies are required at different centers by different research groups to establish the efficacy of PRP over long term follow up period, and multicenter randomized controlled trial would further strengthen evidence-based practice in treatment of LE or tennis elbow.

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