Section: Orthopaedics

Original Research Article

A RANDOMIZED CONTROLLED STUDY TO ANALYZE THE EFFICACY OF LOCAL INJECTION OF AUTOLOGOUS PLATELET-RICH PLASMA IN THE TREATMENT OF LATERAL EPICONDYLITIS COMPARED TO LOCAL CORTICOSTEROID INJECTION

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Corresponding Author:
Dr. Naveenkumar Kuppan,
Email: dgonnaven@gmail.com.

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Erlapati Naga Venkata Ganesh[1], Probin Joseph[2], Naveenkumar Kuppan[3], Manikandan Kumarasamy[4]

[1]Junior resident, Department of Orthopaedics, Sree Manakula Vinayagar Medical College & Hospitals, Puducherry, India.
[2]Assistant Professor, Department of Orthopaedics, Sree Manakula Vinayagar Medical College & Hospitals, Puducherry, India.
[3]Assistant Professor, Department of Orthopaedics, Sree Manakula Vinayagar Medical College & Hospitals, Puducherry, India.
[4]Associate Professor, Department of Orthopaedics, Sree Manakula Vinayagar Medical College & Hospitals, Puducherry, India.

Abstract

Background: Lateral epicondylitis or Tennis Elbow is one of the most common causes of upper extremity pain, with various treatment options. Platelet-rich plasma (PRP) offers a new option for treating lateral epicondylitis. This study compared the efficacy of PRP versus triamcinolone local injection in patients with lateral epicondylitis. **Materials and Methods:** Forty patients with lateral epicondylitis were included in the study and randomized into two groups. Group A was treated with a single injection of 1ml PRP with an absolute platelet count of at least 1 million platelets/ cu.mm. Group B was treated with 1ml (40mg) of triamcinolone acetate. Pain, functional improvements and complications were assessed using a visual analogue scale and Patient-Rated Tennis Elbow Evaluation (PRTEE) score at baseline, one week, six weeks, three months and six months. **Results:** Forty patients completed the follow-up. All assessment parameters improved significantly in both the groups at each follow-up compared to baseline. At the end of six months, Group A showed significantly better improvement than Group B. **Conclusion:** PRP and Triamcinolone acetate effectively treat chronic lateral epicondylitis. However, PRP is a superior treatment option in terms of longer duration of efficacy.

INTRODUCTION

Lateral epicondylitis, commonly known as Tennis Elbow, is one of the most common causes of musculoskeletal pain involving the common extensor origin of the forearm. The pathology arises from repetitive manual work involving wrist and finger extensors, overexertion of the dominant hand and significant disability in daily activities. Discomfort increases with resisted wrist extension with the elbow in 90-degree flexion, resisted forearm supination and while grasping heavy objects. Clinically, tenderness is pointed at the lateral epicondyle region.[1] Diagnosing lateral epicondylitis is straightforward, yet there has been no consensus on the optimal treatment strategy.[2] Local steroid injection is the most preferred treatment option after physiotherapy and has shown to be consistent and predictable in short-term pain relief.[3] Triamcinolone, a highly selective glucocorticoid, suppresses the inflammatory response by attenuating increased capillary permeability and local exudation and decreases the production of pro-inflammatory mediators like prostaglandins, leukotrienes, platelet-activating factor (PAF) through indirect inhibition of phospholipase A2. Recent treatment options include local platelet-rich plasma (PRP) injection, autologous blood, and prolotherapy.[4-6] Platelet-rich plasma is a concentration of platelets derived from the patient's blood. PRP contains various growth factors that build-up reparative processes. The benefits of PRP therapy are hypothesized to include angiogenesis, an increase in growth factor expression, cell proliferation, an increase in the recruitment of repair cells and tensile strength. However, studies on lateral epicondylitis with PRP treatment have yielded inconclusive results.[7-9] Hence, this study explored PRP's efficacy in tennis elbow patients. The study's

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main objective was to compare the efficacy of local platelet-rich plasma injection versus corticosteroids in pain relief and functional improvement in lateral epicondylitis.

MATERIALS AND METHODS

A prospective hospital-based pre- and post-interventional randomized controlled trial on the clinical efficacy of local PRP injection versus corticosteroids in chronic lateral epicondylitis cases was carried out between October 2020 and April 2022. Ethical clearance from the human ethics committee was obtained before the commencement of the study. Forty patients of both genders above 18 years of age suffering from chronic lateral epicondylitis who have failed three weeks of conservative treatment were recruited for the study after obtaining written informed consent. The diagnosis was made based on clinical signs and symptoms. The duration of the symptoms ranged from one to six months. Recruited patients were either on conservative treatment with analgesics and anti-inflammatory drugs or no treatment. A two-week washout period was given to all the patients on analgesics and anti-inflammatory drugs. Patients with a history of arthritis, trauma or fracture, nerve entrapment around the elbow, previous injections, systemic steroid usage, bleeding disorder and psychiatric disorder were excluded from the study. Complete physical examination and relevant investigations were done, including a complete haemogram, fasting blood sugar (FBS) and plain X-ray of the involved elbow. Selected patients were randomized to 2 groups (A and B) by block randomization technique and were not allowed any other treatment during the study period.

Group A patients received a single injection of PRP (1ml), with an absolute platelet count of 1 million platelets/cu.mm, as confirmed by manual counting. PRP was injected into the common extensor origin at the lateral epicondyle of the humerus under aseptic conditions. PRP was prepared under aseptic conditions as per the procedure standardized in the departmental laboratory. A 9001:2000 ISO-certified R-23 centrifuge was used for platelet concentration. Group B patients received a single injection of corticosteroid (Triamcinolone, 40mg in 1 ml). The site of injection and the technique used were the same in both groups. Post injection, sterile dressing was applied, and the patient was observed for any signs of allergy. Only paracetamol (500 mg) tablets were allowed as rescue medication for one week. After assessment of baseline parameters, the patients were given treatment according to their allotted group and called for follow-up assessment after one week, six weeks, three months and six months after intervention.

Parameters Measured

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.

PRTEE score: Patient-Rated Tennis Elbow Evaluation (PRTEE) is a 15-item questionnaire designed to measure physical function and symptoms in patients with chronic lateral epicondylitis. The PRTEE allows patients to rate their levels of tennis elbow pain and disability from 0 to 10 and consists of 2 subscales, pain and function subscale, respectively. The pain subscale has five items, which uses a numerical scale ranging from 0 to 10, where 0 indicates no pain, and 10 indicates the worst imaginable pain. The function subscale has ten items, with six for specific activities and four for usual activities. This also uses a numerical scale ranging from 0 to 10, where 0 indicates no difficulty, and ten indicates unable to do. Any adverse effect reported by the patients was also recorded.

Statistical Analysis

Statistical Analysis was done using SPSS version 16. The numerical variables such as age, VAS, pain, functional and total pain score were summarized as mean/ standard deviation or median/ IQR for normal and skewed distributed data, respectively. The categorical variables such as gender, history, risk factor and comorbidity profile were categorized as frequency and percentage. The graphical distribution of the variables was done using pie charts, bar charts and box and whisker plots. The numerical values between the two intervention groups were compared using the independent t-test for normally distributed data and the Mann-Whitney U test for skewed data. Similarly, the categorical values between the two intervention groups were compared using the chi-square test. A p-value less than 0.05 was considered significant.

RESULTS

Out of the 40 patients recruited for the study, all completed six months of follow-up, 20 in each group. Group A patients received PRP local injection, and Group B patients received Triamcinolone acetate local injection. The age-wise distribution of the patients who completed the study is depicted in [Table 01/Figure-1]. Most of the patients were between the age of 35 to 45 years. The mean age, gender distribution, laterality and mean duration of symptoms were comparable in patients of Groups A and B [Figure-2].

Pain - Pain was assessed using the VAS. The subjective pain report or the VAS score improved more with corticosteroid injection after one week ($p<0.001$), six weeks ($p<0.001$) and three months ($p=0.038$). However, at the end of six months, improvement in pain was significantly better in the PRP injection group ($p=0.588$) [Table 02/Figure-03].

PRTEE score –Pain and Functional outcomes were measured using the PRTEE score. Relatively fast pain and functional score improvement were

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observed in the corticosteroid groups. This improvement was statistically significant in both groups' follow-up visits except at six months. [Table 03/Figure-04]. This might probably be due to a recurrence of pain in one patient of the corticosteroid group. PRTEE total score showed better improvement ($p < 0.05$) in each parameter at one-week, six weeks, and three months follow-ups from pre-procedure values in both groups. When the groups were compared with each other, group B had statistically significant ($p < 0.05$) and better improvement than Group A at one week, six weeks and three-month follow-up period, while at a six-month follow-up, group A had better improvement in each parameter over Group B. [Table 04 & 05/Figure-05& 06].

Complications

None of the patients had local site infections. One patient had hypopigmentation over a local site for the corticosteroid group, and three patients of the PRP group had persistent pain over six months of follow-up. No recurrence was observed in the PRP group; one patient of the corticosteroid group had a recurrence in the follow-up period, which was treated with physiotherapy and symptoms were reduced. [Table 06].

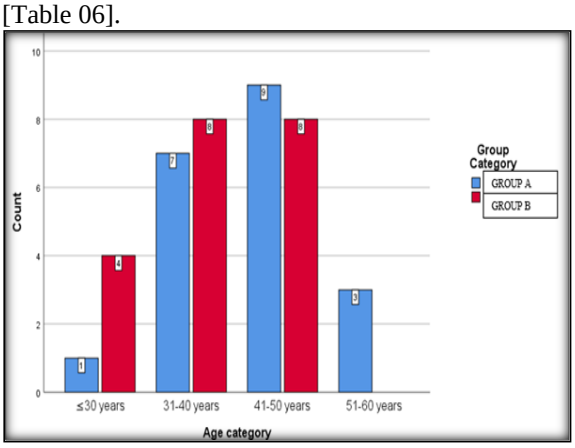

Figure 1: Distribution of age category distribution among the two groups (n=40)

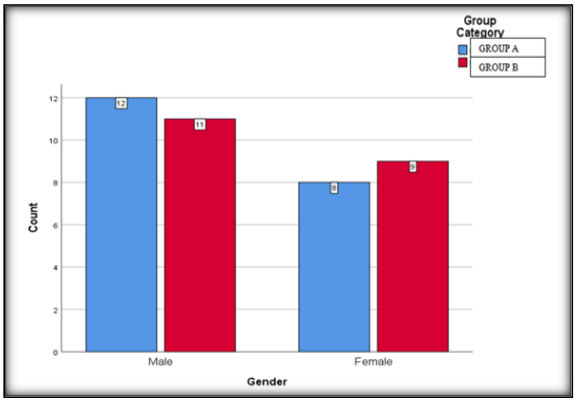

Figure 2: Graphical representation of the gender distribution among the two groups (n=40)

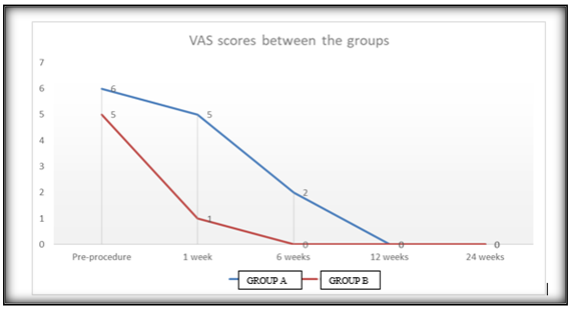

Figure 3: Graphical Comparison of the VAS scores among the two groups at various timelines (n=40)

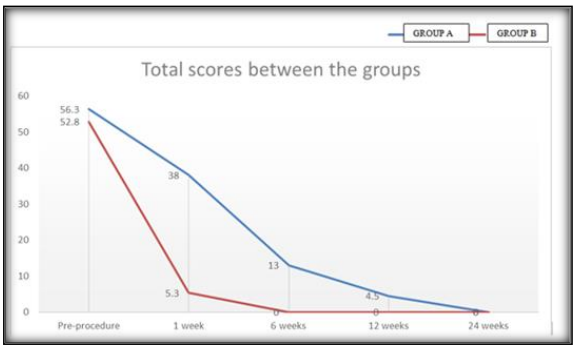

Figure 4: Graphical Comparison of the total PRTEE scores among the two groups at various timelines (N=40)

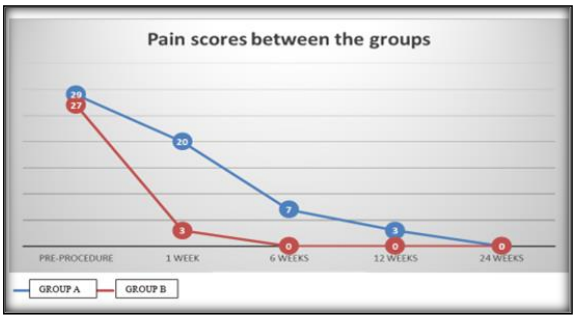

Figure 5: Graphical Comparison of the pain scores among the two groups at various timelines (N=40)

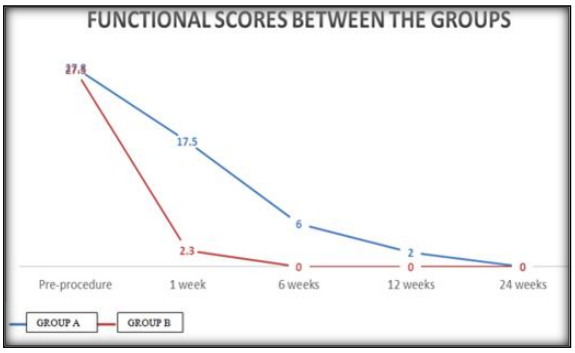

Figure 6: Graphical Comparison of the functional scores among the two groups at various timelines (N=40)

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Table 1: Distribution of cases based on age, gender, side and mean duration of complaints between the two groups (n=40)

Characteristics	Group A	Group B	P-value
Age(years)	42.6	43.4	0.177
Gender(male/female)	12/8	11/9	0.749
Side (Right/Left)	15/5	13/7	0.490
Mean duration of symptoms (months)	3.2	4.6	0.529

Table 2: Comparison of the VAS scores among the two groups at various timelines (N=40)

GROUPS	Base line (pre-procedure)		1 week		6 weeks		3 months		6 months	
	VAS (mean)	P-value	VAS (mean)	P-value	VAS (mean)	P-value	VAS (mean)	P-value	VAS (mean)	P-value
Group A	6.3	0.063	4.1	<0.001	1.8	<0.001	0.4	0.038	0	0.588
Group B	5.6		0.9		0		0		0.5	

Table 3: Comparison of the PRTEE scores among the two groups at various timelines (N=40)

GROUPS	Base line (pre-procedure)		1 week		6 weeks		3 months		6 months	
	PRTEE (mean)	P-value	PRTEE (mean)	P-value	PRTEE (mean)	P-value	PRTEE (mean)	P-value	PRTEE (mean)	P-value
Group A	58.3	0.142	40	<0.001	16.5	<0.001	5.4	<0.001	0.7	0.948
Group B	51.9		7.6		0.6		0.2		4.1	

Table 4: Comparison of the pain scores among the two groups at various timelines (N=40)

GROUPS	Base line (pre-procedure)		1 week		6 weeks		3 months		6 months	
	Pain score (mean)	P-value	Pain score (mean)	P-value	Pain score (mean)	P-value	Pain score (mean)	P-value	Pain score (mean)	P-value
Group A	30.4	0.108	21.7	<0.001	9.4	<0.001	3.3	<0.001	0.4	0.968
Group B	26.1		4.1		0.3		0.2		2.5	

Table 5: Comparison of the functional scores among the two groups at various timelines (N=40)

GROUPS	Base line (pre-procedure)		1 week		6 weeks		3 months		6 months	
	Functional score (mean)	P-value	Functional score (mean)	P-value	Functional score (mean)	P-value	Functional score (mean)	P-value	Functional score (mean)	P-value
Group A	27.9	0.327	18.3	<0.001	7.1	<0.001	2.1	<0.001	0.3	0.968
Group B	25.7		3.5		0.3		0.1		1.6	

Table 6: Shows complications in the study population

Complication	Number of patients affected	Group
Residual pain	3	A
Hypopigmentation	1	B
Local site infection	Nil	Nil
Recurrence	1	B

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Table 7: Comparison of VAS and PRTEE scores of various studies with our study

Study	VAS	PRP			Corticosteroid		
		Pre procedure	12 weeks	24 Week	Pre procedure	12 weeks	24 week
Our study		6.3	0.4	0	5.6	0	0.5
Gosens T et al[54]		6.9.0+/-.59	4+/-.75	3.2 +/-.3	6.6.2 +/-.14	4.5 +/-.27	5.5 +/-.24
Yadav T et al[56]		7.6	1.6	-	7.7	2.8	-
Peer booms et al[60]		7.1 ± .15	3.8 ± .27	5.6+/-.23	6.5 ± .13	4.4 ± .27	3.2+/-.31
	PRTEE						
Our study		58.3	5.4	0	51.9	0.2	0.5
Palacio EP et al[59]		47.1	13.0	0	42.9	21.8	0
Mishra AK et al[58]		54.15	27.05	16.17	57.71	28.88	21.06

DISCUSSION

Lateral epicondylitis, also known as Tennis elbow, is one of the most perplexing disorders of the musculoskeletal system. Tennis elbow probably results from overuse or repetitive micro-trauma resulting in primary tendinosis of the extensor carpi radialis brevis (ECRB) muscle with or without the involvement of extensor digitorum communis (EDC) and extensor carpi radialis longus (ECRL). Repeated dorsiflexion, pronation, and supination in their daily or professional work are the most common causative factors. A female preponderance has been reported in some studies.[10,11] However, Shiri R et al. found a 1.3% prevalence of lateral epicondylitis without any gender difference.[12] The findings of our study support a male preponderance. Chard MD and Hazelman BL reported that lateral epicondylitis more frequently involves the dominant arm and has equal incidence among all socioeconomic classes.[13]

Similar findings are reflected in the results of our study. Various conservative and non-invasive modalities have been tried with inconsistent and non-satisfactory results. Recent studies on chronic lateral epicondylitis have not found any significant evidence of an inflammatory process; hence, the term lateral epicondylitis has been suggested. Nirschl et al. found mainly fibro-elastic tissue and vascular invasion, describing this condition as "angiofibroblastic tendinosis".[14] In recent years, local site injections were performed more than arthroscopic or open surgical procedures as they provided more reasonable and satisfactory results. Therefore, local injection of steroids offers short-term symptomatic relief only, and other treatment options must be explored for long-term relief and remedy of the disease process. In this context, recent literature reviews PRP as a better treatment option. Local corticosteroid injection is one of the most common invasive interventions with consistent and satisfactory results. Hence, it has been used as the gold standard for comparison of newer therapies. Altay et al. reviewed 13 randomized controlled trials and found that corticosteroid injection is effective in pain relief and improving grip

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strength compared to conventional therapies.[15] The exact mechanism of action of local steroid injection is uncertain. Studies suggest that the anti-inflammatory effect of corticosteroids is exerted by suppressing the granulomatous response in traumatized tissue and helps to alleviate pain.[16-18] They also inhibit fibroblast and ground substance protein proliferation.[19]

On the other hand, PRP is an ideal autologous biological blood-derived product that releases high concentrations of platelet-derived growth factors on injection, which helps in tissue healing by cellular differentiation and proliferation, angiogenesis, tissue debris removal, chemotaxis, and ECM formation. Various growth factors and cytokines in PRP include Platelet Derived Growth factors (PDGF-aa, PDGF-bb, PDGF-ab), Transforming Growth Factor beta (TGF-b1, TGF-b2), Fibroblast growth factor (FGF), Insulin-Like Growth Factor-1 and 2 (IGF-1, IGF-2), Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGF), Interleukin – 8 (IL-8), Keratinocyte Growth Factor, Connective Tissue growth factor.[20] Platelets release more than 95% of the pre-synthesized growth factors within one hour of activation. This initial burst is followed by steady synthesis and secretion of growth factors for their remaining life span.[21] The present study, therefore, is an attempt to compare the clinical efficacy of PRP versus corticosteroids. Mishra et al,[7] and Gosens T et al,[22] compared the effectiveness of leukocyte-enriched PRP to standard corticosteroid treatment for lateral epicondylitis and found that at short-term follow-up, both groups showed significant improvement in pain and function. However, over long-term follow-up, pain and functional scores returned to baseline for the corticosteroid group, while that for the PRP group remained high. We observed a long-term effect of steroids in almost all cases for six months, and a recurrence was noted in only one patient in the fifth month of follow-up. [Table 07].

A recent double-blind, randomized control study by Omar a S et al. has reported that the effect of corticosteroid injections lasts for about three months while that of PRP injections lasts for more than six months in providing pain relief in tennis elbow and plantar fasciitis.[23] Our study also shows significant improvement in the corticosteroid group at one week, six weeks and three months, while the PRP group showed significantly more improvement in all outcome measures at a six-month follow-up, which is consistent with the work of Gosens T et al. and Kamezi et al.[22,24]

CONCLUSION

Triamcinolone, a corticosteroid, showed immediate effects in lateral epicondylitis and faster improvement in VAS, pain and function scores compared to PRP. While PRP showed consistent results at the final follow-up and better outcomes in long-term visits. We recommend more extended follow-up studies to substantiate our findings further and establish PRP's long-term efficacy in lateral epicondylitis.

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