RESEARCH PAPER

OUTCOME IN THE MANAGEMENT OF LATERAL EPICONDYLITIS BETWEEN LEUKOCYTE RICH PLATELET RICH PLASMA AND LEUKOCYTE POOR PLATELET RICH PLASMA - A COMPARATIVE STUDY.

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ABSTRACT

Objectives: This study aims to compare the effect of leukocyte concentration in platelet-rich plasma (PRP) on pain, functionality and post-injection local inflammatory reactions in patients with lateral epicondylitis.

Patients and methods: The study included 30 patients (14 males, 16 females; mean age 38.6 years; range 18 to 75 years) with lateral epicondylitis related pain visual analog scale (VAS) score of ≥5 for more than three months. Patients were randomly assigned into three groups. Normal saline (1.5 mL) was injected in group 1 (control group) while a single dose of leukocyte-poor-PRP (1.5 mL) and leukocyte-rich-PRP (1.5 mL) were injected in groups 2 and 3, respectively. An exercise program was recommended to patients in all three groups. Patients were assessed according to VAS, Patient-Rated Tennis Elbow Evaluation, grip dynamometer and pinchmeter, extensor tendon thickness and cortical derangement at baseline and at fourth and eighth weeks after therapy. All patients were questioned regarding paracetamol use and adverse effects after therapy.

Results: No significant differences were detected between groups regarding VAS, Patient-Rated Tennis Elbow Evaluation, grip and pinch measurements, extensor tendon thickness and cortical derangement . In intra-group comparisons, VAS and Patient-Rated Tennis Elbow Evaluation scores obtained at fourth and eighth weeks were significantly decreased in all groups when compared to baseline values . Again, there was no significant difference in the control visit at eighth week when compared to baseline. Assessment of grip and pinch measurements revealed that values obtained at fourth and eighth weeks were significantly increased compared to baseline in all three groups.

Conclusion: According to our study findings, lateral epicondylitis does not seem to affected either leukocyte-rich-PRP or leukocyte-poor-PRP on pain and function in the short term. Leukocyte concentration had no association with post-injection local inflammatory reactions.

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INTRODUCTION

Lateral epicondylitis, also known as tennis elbow, is the most commonly diagnosed cause of pain at lateral aspect of elbow(1).Tennis elbow is considered as an overuse injury of extensor tendons with repetitive micro-trauma(2).Various treatment modalities have been suggested for lateral epicondylitis including resting, non-steroidal antiinflammatory drugs, physical therapy, extracorporeal shock wave therapy, ultrasound therapy, botulinum injection, and corticosteroid injection. Surgical release may be needed in recalcitrant cases. Injection of biological agents such as platelet-rich plasma (PRP) achieves a favorable long-term clinical outcome(3). Platelet-rich plasma is an autologous blood product which contains concentrated platelets. Experimentally, PRP promotes tendinous healing through release of different growth factors.

This treatment can optimize healing in pathological human tendons(4).There is no standard technique for the preparation of PRP. It can be prepared manually and there are also various commercial PRP.In average, PRP has three- to five-fold higher platelet count compared to whole blood. There are no widely accepted and quantified values of platelet concentrations in PRP(5,6).There are four types of PRP; each of them has two subtypes based on the platelet and leukocyte counts as well as activation of PRP (Table 1).

The use of leukocyte-rich (type 1) PRP (LR-PRP) may produce a more intense local inflammatory response and be associated with an increased post-injection pain response(7-10).In this study, we aimed to compare the effect of leukocyte concentration in PRP on pain, functionality and post-injection local inflammatory reactions in patients with lateral epicondylitis.

PATIENTS AND METHODS

This double-blinded, randomized, controlled study comparing the effects of LR and leukocyte-poor PRP (LP-PRP) on function and pain in patients with lateral epicondylitis was conducted Department of Orthopaedics, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai, Tamil Nadu, India. This was a prospective comparative observational study carried out over a period of 12 months from March 2025 to February 2026.The study was conducted on 30 patients (14 males, 16 females; mean age 38.6 years; range 18 to 75 years) who were suffering from pain associated with lateral epicondylitis for

more than three months (visual analog scale [VAS] ≥5). Pregnant females, patients with cervical radiculopathy or carpal tunnel syndrome, peripheral nerve injury, thrombocytopenia or other coagulation disorder, those receiving anticoagulant therapy, those with systemic diseases such as diabetes, rheumatoid arthritis or other inflammatory arthritis (such as psoriatic arthritis, ankylosing spondylitis), hepatitis, those who underwent steroid injections within three months prior to the study and those who received physical therapy and rehabilitation program for lateral epicondylitis within six months prior to the study were excluded.The study protocol was approved by the Ethics Committee. A written informed consent was obtained from each patient.

The diagnosis of lateral epicondylitis was primarily made based on patients' history and clinical examinations. Patients with at least one positive test (Mill's test, Cozen's test, Maudsley test) were included. Erythrocyte sedimentation rate, C-reactive protein, complete blood count and biochemistry tests were ordered from the patients. Plain radiographs of lateral epicondylitis were usually normal. Pre-arch and lateral elbow radiographs were performed to demonstrate soft tissue calcifications and establish a differential diagnosis

Patients were randomly assigned into three groups (n=10 in each) by using the block randomization method. Both the patient and investigator were blinded to the treatment given. Normal saline (1.5 mL) was injected to the patients in group 1 (control group) while LR-PRP (1.5 mL) and LP-PRP (1.5 mL) were injected to the patients in groups 2 and 3 via peppering technique at the most sensitive point, respectively. Peppering technique involves insertion of a needle into the tendon to inject some of the blood; followed by retraction of the needle to subcutaneous tissue and redirection and reinsertion of the needle. In this study, the injections were performed without ultrasound guidance.

Manual PRP preparation techniques were used in this study. According to the system instructions, blood (16 mL) was drawn from cubital vein; then, citrate (4 mL) was added to prevent premature clotting. Following placement of blood samples in 10 mL tubes, the LP-PRP was centrifuged at 1075 rpm for 15 minutes in the first step. Then, it was re-centrifuged at 1495 rpm for 15 minutes under layer 1 and layer 2 of laminar flow. Following centrifugations, the platelets were initially collected by a poor plasma syringe and these platelets were not used for injection. Thereafter, the remaining platelets were collected from the tube and two aliquots containing approximately 1.5 mL of PRP were obtained. Of these, one was injected to the patient while the other was used to determine cell count. After receiving the same amount of blood for LR-PRP, the blood was centrifuged at 1190 rpm for 20 minutes in the first step. Then, it was re-centrifuged for 15 minutes at 1890 rpm in the second step. The platelet concentration was intended to be two- or eight-fold higher than the basal value while the leukocyte concentration was intended to be three-fold lower and three-fold higher than the basal value in the LP-PRP and LR-PRP groups, respectively

In all groups, an exercise program was prescribed including three sets per day consisting of 10 repetitive range of motion, stretching, strengthening, and gripping exercises for over four weeks. The exercise program was initiated on the second day after injection. The patients were given brochures containing a written statement. Patient compliance of the exercise program was recorded. Non-steroidal antiinflammatory drug use was prohibited for one week before and after PRP application. The use of paracetamol up to 4 g/day for pain before and after injection was allowed.

At baseline and on the fourth and eighth weeks after treatment, the patients were evaluated by using VAS, patient-based forearm questionnaire, flu dynamometer and pinch measurements, extensor tendon thickness and cortical irregularity. Jamar type Saehan brand (Saehan Corp. Masan, Korea) hydraulic hand dynamometer was used to assess the maximum gripping force, which was recorded as libra unit. A hydraulic pinchmeter same brand as hand dynamometer was used to evaluate finger grip strength. The extensor tendon thickness was calculated by measuring the maximum thickness in the sagittal plane using a superficial linear probe with a Toshiba Aplio 500 (Toshiba Co. Ltd. Tokyo, Japan) sonography device by the same physician blinded to the treatment. The patients were questioned for paracetamol use and side effects (swelling, redness, and/or soreness) after treatment

RESULTS

In the control group, the dominant arm was affected in 8 of 10 patients with right arm dominance and 9 of 10 patients with right arm dominance in LP-PRP and LR-PRP groups, respectively. Table 2 presents data distribution of demographic characteristics. In this study, no significant difference was found between the groups regarding visual analog scale, patient-based forearm assessment questionnaire, daily life questionnaire, flu and pinch measurements, extensor tendon thickness and cortical irregularity ($p>0.05$). In intragroup comparisons, visual analog scale and patient-based forearm evaluation questionnaire scores were significantly lower on the fourth and eighth weeks after injection when compared to baseline in all groups.

No significant decrease was observed on the eighth week when compared to the results obtained on the fourth week after injection .When the grip and pinch measurements were evaluated, significant improvement was detected on the fourth and eighth weeks when compared to baseline in the PRP and control groups .In addition, a significant improvement was observed on the eighth week when compared to the fourth week after injection in LR-PRP group. There was no significant increase in other groups. When the extensor tendon thickness was assessed, no significant reduction was observed in any group. There was no difference in paracetamol use and post-injection reactions (swelling, redness, and/or soreness) among groups.

Table 1. Distribution by demographic characteristics

	Control group	LP-PRP group	LR-PRP group	

	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	
Age (year)			47.6+/-9.1	46.50	30-67			45+/-8.6	46	28-60			46.5+/-8.6	45	21-67	
Sex																
Woman	4	40				6	60				6	60				
Male	6	60				4	40				4	40				
Affected arm																
Right	8	80				9	90				9	90				
left	2	20				1	10				1	10				
Dominant arm																
Right	10	100				10	100				10	100				
left	0	0				0	0				0	0				

LP-PRP: Leukocyte-poor platelet-rich plasma; LR-PRP: Leukocyte-rich platelet-rich plasma; SD: Standard deviation; Min: Minimum; Max: Maximum.

Comparison of visual analog scale scores across groups

	Control group			LP-PRP group			LR-PRP group		
	Mean±SD Median Min-Max			Mean±SD Median Min-Max			Mean±SD Median Min-Max		
VAS (nocturnal) before therapy	***6.7+/-1.9***	***7***	***3-10***	***7.3+/-2.2***	***8***	***3-10***	***6.6+/-2.3***	***7***	***0-10***
VAS (night) 4th week	***4.1+/-2.6***	***4.5***	***0-8***	***3.6+/-3.1***	***4***	***0-9***	***4.6+/-3.1***	***5***	***0-10***
VAS (nocturnal) 8th week	***3.5+/-2.99***	***4.5***	***0-10***	***3.5+/-2.99***	***4.5***	***0-10***	***3.3+/-3.3***	***2***	***0-10***
p*									
VAS (motion) before therapy	***8.1+/-1.8***	***9***	***5-10***	***8.7+/-1.7***	***10***	***4-10***	***7.8+/-1.9***	***8***	***3-10***
VAS (motion) 4th week	***5.8+/-3.3***	***6***	***0-10***	***5.5+/-2.7***	***5***	***2-10***	***5.9+/-2.8***	***5***	***0-10***
VAS (motion) 8th week	***5.1+/-3.3***	***5***	***0-10***	***5.1+/-3.0***	***5***	***0-10***	***4.4+/-3.3***	***3.5***	***0-10***
p*									

LP-PRP: Leukocyte-poor platelet-rich plasma; LR-PRP: Leukocyte-rich platelet-rich plasma; VAS: Visual analog scale; SD: Standard deviation; Min: Minimum; Max: Maximum; * before therapy min-max values; † 4th week min-max values; ‡ 8th week min-max values.

Discussion

The present study evaluated the effectiveness of single-dose leukocyte-poor platelet-rich plasma (LP-PRP) and leukocyte-rich platelet-rich plasma (LR-PRP) compared with normal saline in patients with lateral epicondylitis. Our findings demonstrated that neither LP-PRP nor LR-PRP was significantly superior to normal saline in terms of pain reduction or functional improvement during the short-term follow-up period. Although significant improvements were observed in some functional parameters within the treatment groups, these improvements did not result in statistically significant differences between the groups. These findings add to the existing evidence suggesting that the clinical efficacy of PRP in lateral epicondylitis remains controversial and may be influenced by the duration of follow-up, number of injections, preparation technique, platelet concentration,

leukocyte concentration, and characteristics of the patient population.

The conflicting evidence regarding PRP is illustrated by the study of Montalvan et al., in which patients with lateral epicondylitis received two PRP injections at an interval of four weeks, while the control group received normal saline. Pain was assessed at 1, 3, 6, and 12 months. Although both groups demonstrated significant improvement in pain scores over time, there was no significant difference between the PRP and saline groups at the subsequent follow-up assessments. These findings suggest that improvement may occur as part of the natural course of lateral epicondylitis and that the injection procedure itself may have a therapeutic or placebo effect.5

In contrast, Mishra et al. reported more favorable long-term results with LR-PRP. In their randomized controlled study, 230 patients with chronic lateral epicondylitis were included, with 116 patients receiving LR-PRP and the remaining patients receiving control treatment. At 12 weeks, there was no significant difference in visual analogue scale scores between the groups. However, at 24 weeks, the LR-PRP group demonstrated significantly greater improvement compared with the control group.6 This observation raises an important question regarding whether the therapeutic effect of PRP may become more apparent only after a prolonged period. The delayed improvement observed in that study may be related to the time required for PRP-associated growth factors to influence tendon remodeling and healing.

The difference between the findings of Mishra et al. and those of the present study may therefore be partly explained by the duration of follow-up. Tendon healing is a gradual biological process involving cellular proliferation, extracellular matrix production, collagen remodeling, and maturation. PRP is believed to promote these processes through the release of several growth factors and cytokines. Consequently, a single PRP injection may not produce an immediate clinical benefit, particularly in chronic tendinopathy where structural degeneration and failed healing predominate.6 A longer follow-up period may therefore be necessary to determine whether the initial lack of superiority of PRP over saline persists over time.

Our findings are also comparable with those of Krogh et al., who conducted a randomized, double-blind, placebo-controlled trial involving 60 patients with lateral epicondylitis. Patients were randomized to receive PRP, corticosteroid, or saline injection and were evaluated over a three-month period. Neither PRP nor corticosteroid demonstrated a superior effect on pain and function compared with saline at the primary endpoint.7 The similarity between that study and the present study is notable because both used saline as a placebo comparator and evaluated the effects of treatment over a relatively short period. These findings suggest that the beneficial effects observed following PRP injection in the early postoperative or post-injection period may not necessarily be attributable to the biological action of PRP itself.

An important component of the present study was the comparison between LP-PRP and LR-PRP. Despite the theoretical differences in their biological composition, no significant differences were identified between the two PRP preparations with respect to pain, functional outcomes, or local inflammatory reactions. The role of leukocytes in PRP therapy remains controversial. Leukocytes may contribute to tissue repair through immunomodulatory, antimicrobial, and angiogenic mechanisms. Conversely, excessive leukocyte concentrations may increase the inflammatory response and potentially cause greater post-injection pain, swelling, and local irritation. Therefore, the optimal leukocyte concentration in PRP remains uncertain.

The possible importance of long-term follow-up is further supported by the study of Gautam et al., who compared LR-PRP with corticosteroid injection in patients with recalcitrant lateral epicondylitis. Patients were evaluated at the second week, sixth week, third month, and sixth month. The authors reported significant improvement in the LR-PRP group at six months compared with baseline, particularly with respect to functional outcomes and grip strength.8 These findings suggest that PRP may have a delayed beneficial effect that becomes more evident during the later stages of tendon healing.

In the present study, significant improvement was observed at the eighth week compared with the fourth week in grip and pinch strength measurements in the LR-PRP group. However, the absence of a significant difference between the treatment groups indicates that these improvements cannot be conclusively attributed to PRP. Recovery may also have been influenced by the natural history of lateral epicondylitis, rehabilitation, activity modification, or the nonspecific effects of injection. Nevertheless, the progressive improvement in grip and pinch strength observed in the LR-PRP group warrants further investigation using longer follow-up periods.

Another important finding was the absence of a significant difference between LP-PRP and LR-PRP regarding local inflammatory responses. Patients were specifically assessed for post-injection swelling and redness, but no significant differences were detected between the groups. Riboh et al. evaluated the influence of leukocyte concentration on the efficacy and safety of PRP and reported that LP-PRP and LR-PRP did not demonstrate substantial differences in efficacy or safety in their analysis.9 These findings suggest that leukocyte concentration alone may not determine the clinical response or degree of local inflammation following PRP administration.

The lack of standardization in PRP preparation remains an important limitation when comparing studies. Different studies use different platelet concentrations, leukocyte concentrations, activation methods, injection volumes, preparation systems, and numbers of injections. Therefore, PRP should not be regarded as a single standardized biological treatment. Variations in the cellular composition of PRP may substantially influence its biological effects and clinical outcomes. Standardized reporting of platelet and leukocyte concentrations is therefore essential for meaningful comparison between studies.

The present study has several clinical implications. Our results suggest that a single injection of either LP-PRP or LR-PRP should not be considered superior to normal saline for short-term improvement in pain and function in patients with

lateral epicondylitis. However, the possibility of a delayed therapeutic effect cannot be excluded. Future randomized controlled trials should include longer follow-up periods, standardized PRP preparation protocols, precise reporting of platelet and leukocyte concentrations, and objective assessment of tendon healing. Further studies are also required to determine whether repeated PRP injections or specific leukocyte concentrations provide superior long-term outcomes.

Overall, the findings of the present study indicate that PRP did not demonstrate a significant short-term advantage over placebo in patients with lateral epicondylitis. Although improvements in functional parameters were observed, particularly in grip and pinch strength, these changes were not significantly different between treatment groups. The available evidence therefore suggests that the role of PRP, and particularly the influence of leukocyte concentration, remains uncertain. Longer-term, adequately powered randomized studies with standardized PRP preparation are necessary to establish its true therapeutic value.

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