



Original Research Article

Does leucocyte concentration have a role in the outcome of PRP therapy for lateral epicondylitis – A randomized controlled trial

Sadhan Palakuri^{1,*}, Sathish Muthu²¹Apollo Healthcity, Jubilee Hills, Hyderabad, Telangana, India²Orthopaedic Research Group, Coimbatore, Tamil Nadu, India

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ABSTRACT

Background: Of late the leucocyte concentration in the platelet-rich plasma (PRP) therapy for lateral epicondylitis has gained importance. We aimed to evaluate the effects of leucocyte concentration in the outcomes of the PRP used for lateral epicondylitis.

Materials and Methods: This is a double-blinded randomized controlled trial conducted on patients having lateral epicondylitis comparing the pain relief and functional effects of leucocyte-poor PRP (LP-PRP) and leucocyte-rich PRP (LR-PRP) at one, three, six, and twelve months post-injection using the Visual Analog Scale (VAS) for pain and Mayo Elbow Performance Score (MEPS) for function.

Results: A total of 85 patients were randomized into LP-PRP (n=42) and LR-PRP (n=43) with a mean age of 49.67 (SD=11.9) and M:F = 1.34. The pre-treatment VAS between the LP-PRP and LR-PRP groups were 8.83±0.7 and 9.12±0.63 respectively while the pre-treatment MEPS were 44.81±8.6 and 45.45±5.43 respectively. We noted significant improvement in the pain and functional scores in both the groups at all observed time frames compared to their pre-treatment measures. However, we did not find any significant difference in the MEPS between the groups nor the difference in the VAS found between the groups at 1 year follow-up was more than the minimal clinically important difference (MCID) for the scale utilized. No significant difference in the complication rate was noted between either of the groups.

Conclusion: PRP injections are a safe and effective treatment method in the management of patients with lateral epicondylitis irrespective of the concentration of the leucocytes present in them. We have established that the concentration of leucocytes did not play a role in altering the course of the treatment outcome.

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1. Introduction

Regenerative medicine has paved the way for less invasive techniques, minimal morbidity, and percutaneous administration of biological substances with osteoinductive and osteoconductive properties.¹ Platelet-rich plasma (PRP) injection has evolved as a big boon in the treatment of musculoskeletal disorders. The usage of autologous PRP for the management of lateral epicondylitis was increasing among orthopedic surgeons and regenerative orthobiologists.² Extensive researches were conducted on the biomolecules that present in PRP to trace the mechanism

involved in alleviating the disease process in lateral epicondylitis.³ There was no consensus on the technique of PRP preparation, the type of PRP to be used, the dose and frequency of PR injection and the amount of growth factors to be delivered at the pathological site for various diseases.^{4–6}

A controversy on the usage is use of either leucocyte rich or leucocyte poor PRP for lateral epicondylitis. Leucocyte content in PRP solution modulates inflammation through secretion of inflammatory cytokines and matrix metalloproteinases which exaggerate an inflammatory response at the site of action.⁷ Lana et al.⁸ devised MARSPILL classification to identify the variables responsible for the therapeutic action of PRP. Leucocyte-

* Corresponding author.

E-mail address: dr.sadhanpalakuri@gmail.com (S. Palakuri).

rich PRP (LR-PRP) elicits a catabolic, inflammatory, and detrimental environment while Leucocyte-poor PRP (LP-PRP) elicits an anabolic effect on the tissues being injected.⁹ In acute pathologies, LR-PRP helps in inflammatory regeneration and early angiogenesis at the injury site whereas LR-PRP in chronic pathologies leads to the formation of scar tissue at the injury site.¹⁰ The histological evaluation of chronic tendinopathies of the animal model demonstrated that large collagen fibril formation with LP-PRP. The usage of LR-PRP in osteoarthritis (OA) knee in vivo and in vitro demonstrated the detrimental effect of cartilage by increasing pro-inflammatory cytokines and anti-catabolic properties.⁹

There is no scientific evidence available for the usage of the right type of PRP (LR-PRP or LP-PRP) to treat lateral epicondylitis. We aimed to evaluate the effects of leucocyte concentration in the outcomes of the PRP used for lateral epicondylitis.

2. Materials and Methods

This is a prospective double-blinded randomized controlled study conducted in clinically diagnosed lateral epicondylitis. Patients in the age group between 18-65 years were included in the study. All the cases were clinically diagnosed. Patients with thrombocytopenia with a platelet count of $<10^5/\text{ul}$, septicemia, local infections, consistent use of nonsteroidal anti-inflammatory drugs within 48 hours of the procedure, or corticosteroid injection at the site of treatment or the use of systemic corticosteroids within a month were excluded from the study.

All patients enrolled in the study were divided into two groups, Group A who received the LR-PRP, and Group B who received LP-PRP. The PRP was infiltrated by a single physician using an aseptic technique. We used 1.5ml of a dual-spin leucocyte-rich variant of the PRP for patients of Group A and 1.5 ml of a dual-spin leucocyte-poor variant of the PRP for patients with Group B. The clinical outcome of the patients was evaluated using Visual Analogue Score (VAS) for pain and functional outcome using Mayo Elbow Performance Score (MEPS) measured pre-intervention and 1 month, 3 months, 6 months, and 12 months post-intervention.

We used IBM SPSS Version 25 (Chicago, Illinois) for statistical analysis. Mean and standard deviations (SD) were used for the presentation of continuous variables and proportions were used for nominal variables. We used the Shapiro-Wilk normality test to the data obtained to check for normality. A paired student t-test was used for comparison of the functional outcome measures pre-and post-intervention and chi-square test for between-group comparisons. A p-value of less than 0.05 was considered statistically significant.

3. Results

A total of 85 patients were randomized into LP-PRP (n=42) and LR-PRP (n=43) with a mean age of 49.67 (SD=11.9) and M:F = 1.34. We did not note any significant difference between the two groups with regard to their general characteristics such as age, duration of the disease as given in Table 1. The pre-treatment VAS between the LP-PRP and LR-PRP groups were 8.83 ± 0.7 and 9.12 ± 0.63 respectively while the pre-treatment MEPS were 44.81 ± 8.6 and 45.45 ± 5.43 respectively. The patients were serially followed at 1 month, 3 months, 6, and 12 months, and their improvement in VAS and MEPS comparing both the groups were represented in Table 2, Figures 1 and 2 respectively.

We noted significant improvement in the pain and functional scores in both the groups at all time points of follow-up compared to the baseline as shown in Table 3. At 12 months post-intervention the mean VAS score was significantly lower in the LR-PRP group (2.48 ± 1.7) compared to the LP-PRP group (3.69 ± 1.42). However, the difference was not clinically important for the score utilized. We did not find the difference in the VAS to be more than the minimal clinically important difference (MCID) measured between both the groups at 12 months. However, no significant difference was noted between the groups in terms of the functional outcome by MEPS as shown in Table 2. No significant difference in the complication rate was noted between either of the groups.

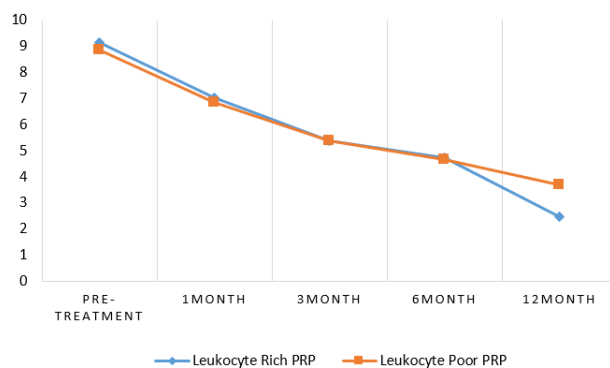


Fig. 1: Comparison of mean VAS score between two groups at various timepoints

4. Discussion

Clinical studies assessing PRP injections in lateral epicondylitis typically do not take into consideration the concentration of leukocytes in operation despite a growing number of clinical trials over time. Several studies have indicated that leukocytes in PRP have positive anti-infectious, immunoregulatory, and angiogenesis effects while some studies have proposed that leukocytes should be withdrawn from PRP and LP-PRP are the ideal candidates

Table 1: General characteristics of the patients included in the study

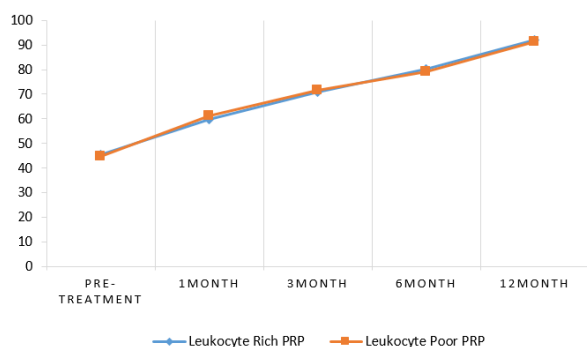
		Leukocyte Rich PRP		Leukocyte Poor PRP	
		Mean	SD	Mean	SD
Age (yrs)		48.67	11.07	50.62	12.85
Duration (months)		4.12	.99	5.40	1.19
Gender	Female	21	48.8%	22	52.4%
	Male	22	51.2%	20	47.6%
Side	Left	18	41.9%	20	47.6%
	Right	25	58.1%	22	52.4%

Table 2: Comparison of mean score of VAS and MEP between the two groups.

		Leukocyte Rich PRP		Leukocyte Poor PRP		Unpaired t-test (p-value)
		Mean	SD	Mean	SD	
VAS	Pre-treatment	9.12	.63	8.83	.70	0.052
	1month	7.00	.70	6.83	.66	0.264
	3month	5.36	.76	5.36	.76	1.00
	6month	4.71	.67	4.64	.69	0.633
	12month	2.48	1.70	3.69	1.42	0.001**
MEPS	Pre-treatment	45.45	5.43	44.81	8.60	0.683
	1month	59.71	3.40	61.17	3.57	0.060
	3month	70.83	4.34	71.69	3.22	0.307
	6month	80.14	6.63	79.00	6.76	0.436
	12month	91.98	10.97	91.21	11.38	0.756

Table 3: Mean comparison of VAS and MEPS at various visits with pre-treatment score.

		Pre-treatment	1 st month	3 rd month	6 th month	12 th month	Paired t-test p-value
		VAS	LR-PRP	9.12 ± 0.63	7.00 ± 0.70	5.36 ± 0.76	4.71 ± 4.64
	LP-PRP	8.83 ± 0.7	6.83 ± 0.66	5.36 ± 0.76	4.64 ± 0.69	3.69 ± 1.42	0.001**
MEPS	LR-PRP	45.45 ± 4.43	59.71 ± 3.40	70.83 ± 4.34	80.14 ± 6.63	91.98 ± 10.97	0.001**
	LP-PRP	44.81 ± 8.60	61.17 ± 3.57	71.69 ± 3.22	79.00 ± 6.76	91.21 ± 11.38	0.001**

**Fig. 2:** Comparison of mean MEPS score between two groups at various timepoints

for the lateral epicondylitis.¹¹

The implications of leukocyte concentration in PRP are not well known. In a study comparing the influence of LR-PRP and corticosteroid on grip measures in patients with lateral epicondylitis by Gautam et al.¹² patients were

assessed in the second week, the sixth week, third month, and sixth month. A substantial increase in the LR-PRP group was observed at the sixth month relative to pre-treatment values. As a result of these effects, they concluded that increasing the concentration of leukocytes in PRP can have a beneficial impact on tendon healing in the long term. This may be attributed to the enhancement of wound healing by increasing the local inflammatory response to leukocytes.

Our study was concurrent with the study results by Yerlikaya M et al.¹³ who showed that superiority was established for either a single dose of LP-PRP or the LR-PRP for lateral epicondylitis. The study showed no significant difference in short-term improvement in pain in both the arms. However, a significant improvement was seen in either of the groups regarding VAS and MEPS in the long term. There was no significant difference in the recurrence between the two groups. Montalvan et al.¹⁴ found improvement in pain scores significantly at the 6th and 12th months in both the groups but no significant differences were detected among groups.

Limitations of the study are that magnetic resonance imaging should have been done pre and post-injection in the affected area for objective radiological quantification of the improvement in the patients. Our study was conducted on small sample size and is a single-center study with a short follow-up. Further studies with a large sample size involving multiple centers are needed to understand the effect of preparation techniques and the method of application of PRP in the long term.

5. Conclusion

PRP injections are a safe and effective treatment method in the management of patients with lateral epicondylitis irrespective of the concentration of the leucocytes present in them. We have established that the concentration of leucocytes did not play a role in altering the course of the treatment outcome.

6. Conflict of Interest

The authors declare no potential conflict of interests.

7. Source of Funding

No funding was utilized for the conduction of the study.

References

- Chen FM, Liu X. Advancing biomaterials of human origin for tissue engineering. *Prog Polym Sci.* 2016;53:86–168.
- Oryan A, Alidadi S, Moshiri A, Maffulli N. Bone regenerative medicine: classic options, novel strategies, and future directions. *J Orthop Surg Res.* 2014;9(1):18. [doi:10.1186/1749-799x-9-18](https://doi.org/10.1186/1749-799x-9-18).
- Mishra AK, Skrepnik NV, Edwards SG, Jones GL, Sampson S, Vermillion DA, et al. Efficacy of platelet-rich plasma for chronic tennis elbow: a double-blind, prospective, multicenter, randomized controlled trial of 230 patients. *Am J Sports Med.* 2014;42(2):463–71.
- Dhurat R, Sukesh MS. Principles and methods of preparation of platelet-rich plasma: A review and author's perspective. *J Cutan Aesthet Surg.* 2014;7(4):189–97. [doi:10.4103/0974-2077-150734](https://doi.org/10.4103/0974-2077-150734).
- Middleton KK, Barro V, Muller B, Terada S, Fu FH. Evaluation of the Effects of Platelet-Rich Plasma (PRP) Therapy Involved in the Healing of Sports-Related Soft Tissue Injuries. *Iowa Orthop J.* 2012;32:150–63.
- Hussain N, Johal H, Bhandari M. An evidence-based evaluation on the use of platelet rich plasma in orthopedics – a review of the literature. *SICOT-J.* 2017;3:57. [doi:10.1051/sicotj/2017/036](https://doi.org/10.1051/sicotj/2017/036).
- Yin W, Qi X, Zhang Y, Sheng J, Xu Z, Tao S, et al. Advantages of pure platelet-rich plasma compared with leukocyte- and platelet-rich plasma in promoting repair of bone defects. *J Transl Med.* 2016;14. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4792107/>.
- Lana J, Purita J, Paulus C, Huber SC, Rodrigues BL, Rodrigues AA, et al. Contributions for classification of platelet rich plasma - proposal of a new classification: MARSPILL. *Regen Med.* 2017;12(5):565–74.
- Yan R, Gu Y, Ran J, Hu Y, Zheng Z, Zeng M, et al. Intratendon Delivery of Leukocyte-Poor Platelet-Rich Plasma Improves Healing Compared With Leukocyte-Rich Platelet-Rich Plasma in a Rabbit Achilles Tendinopathy Model. *Am J Sports Med.* 2017;45(8):1909–20.
- Le ADK, Enweze L, DeBaun MR, Dragoo JL. Current Clinical Recommendations for Use of Platelet-Rich Plasma. *Curr Rev Musculoskeletal Med.* 2018;11(4):624–34. [doi:10.1007/s12178-018-9571-7](https://doi.org/10.1007/s12178-018-9571-7).
- Spaková T, Rosocha J, Lacko M, Harvanová D, Gharaibeh A. Treatment of Knee Joint Osteoarthritis with Autologous Platelet-Rich Plasma in Comparison with Hyaluronic Acid. *Am J Physical Med Rehabil.* 2012;91(5):411–7. [doi:10.1097/ptm.0b013e3182aabb72](https://doi.org/10.1097/ptm.0b013e3182aabb72).
- Gautam VK, Verma S, Batra S, Bhatnagar N, Arora S. Platelet-Rich Plasma versus Corticosteroid Injection for Recalcitrant Lateral Epicondylitis: Clinical and Ultrasonographic Evaluation. *J Orthop Surg.* 2015;23(1):1–5. [doi:10.1177/2309299015023001001](https://doi.org/10.1177/2309299015023001001).
- Yerlikaya M. Comparison of Effects of Leukocyte-Rich and Leukocyte-Poor Platelet-Rich Plasma on Pain and Functionality in Patients With Lateral Epicondylitis. *Arch Rheumatol.* 2018;33(1):73–9. [doi:10.5606/archrheumatol.2018.6336](https://doi.org/10.5606/archrheumatol.2018.6336).
- Montalvan B, Goux PL, Klouche S, Borgel D, Hardy P, Breban M, et al. Inefficacy of ultrasound-guided local injections of autologous conditioned plasma for recent epicondylitis: results of a double-blind placebo-controlled randomized clinical trial with one-year follow-up. *Rheumatol.* 2016;55(2):279–85. [doi:10.1093/rheumatology/kev326](https://doi.org/10.1093/rheumatology/kev326).

Author biography

Sadhan Palakuri, Senior Registrar

Sathish Muthu, Research Associate  <https://orcid.org/0000-0002-2890-869X>

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