

SINGLE INJECTION VERSUS PEPPERING INJECTION TECHNIQUE WITH PLATELET RICH PLASMA IN LATERAL EPICONDYLITIS

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Received : 28/01/2023
Received in revised form : 10/03/2023
Accepted : 24/03/2023

Keywords:

Pepper injection technique, Single injection technique, Platelet rich plasma, Lateral epicondylitis.

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DOI: 10.47009/jamp.2023.5.2.225

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 1065-1070



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Abstract

Background: Autologous Platelet Rich Plasma (PRP) injection is now widely accepted treatment in the treatment of lateral epicondylitis. Prior studies on PRP injection treatment in lateral epicondylitis have not emphasized on the injection technique used to deliver PRP to the site of maximum tenderness on lateral epicondyle. PRP can be delivered by either single injection at the point of maximum tenderness or by pepper injection technique at the point of maximum tenderness. Which injection technique is more effective in treating lateral epicondylitis needs to be further studied. The aim of study was to compare the outcome of treatment of lateral epicondylitis with PRP with single injection technique and pepper injection technique in terms of improvement in functional outcome and pain. **Materials and Methods:** A comparative study was conducted in 62 patients with lateral epicondylitis treated with PRP injection by single injection technique (31 patients) and PRP injection by pepper injection technique (31 patients). Patients were followed up at the 2nd week, 4th week, 8th week and 12th week and assessed with Patient Rated Tennis Elbow Evaluation (PRTEE) Score and Visual Analog Pain Scale (VAS) Score during follow up. Repeated measures of ANOVA was used to determine the statistical significance of scores during follow up in both groups. The mean scores of PRTEE and VAS score with single injection technique were compared with that of pepper injection technique using unpaired t test. **Result:** Repeated measures of ANOVA showed that PRP injection improves mean PRTEE score and mean VAS score during the 2nd week, 4th week, 8th week and 12th week follow up in both single injection and pepper injection group. During follow up period the mean scores of PRTEE and VAS were better with pepper injection technique than single injection technique. Unpaired t test done to compare PRTEE mean scores and VAS mean scores among the two groups found that there is statistically significant difference in mean PRTEE and mean VAS scores during regular follow up interval ($p < 0.001$). The final functional outcome and improvement in pain measured by both PRTEE score and VAS score at 12 weeks was better with pepper injection technique group. **Conclusion:** The functional outcome and improvement in pain was better with pepper injection technique than with single injection technique. So, whenever PRP is used in treatment of lateral epicondylitis, pepper injection technique may be preferred over single injection technique for better functional outcome and improvement in pain.

INTRODUCTION

Autologous Platelet Rich Plasma (PRP) is now widely used in many centers and accepted as treatment of chronic lateral epicondylitis (tennis elbow) and has shown very good results.^[1,2] Lateral epicondylitis is most commonly due to repeated microtrauma to Extensor carpi radialis brevis

(ECRB) tendon origin at the common extensor origin.^[3] It is an overuse injury that can also involve Extensor carpi radialis longus (ECRL) and Extensor carpi ulnaris (ECU).^[4]

Platelet-rich plasma (PRP) contains many Growth factors and mediators like platelet-derived growth factor (PDGF), epidermal growth factors (EGF), transforming growth factor-1 (TGF-1) and vascular

endothelial growth factor (VEGF) which helps in wound healing process when injected to an injury site.^[5] These multiple growth factors and mediators activates intracellular signal transduction system after binding to the target cell receptor resulting in a biological response that is necessary for chemotaxis, cell proliferation and neovascularization.^[6,7] Previous studies on PRP injection treatment in lateral epicondylitis have not emphasized on the injection technique used to deliver PRP to the site of maximum tenderness on lateral epicondyle. PRP can be delivered to the site by single injection technique or by peppering technique.^[8] In single injection technique the entire PRP is injected fully to the site of maximum tenderness in one injection. In peppering injection technique after penetrating the skin at the point of maximal tenderness the needle is inserted up to the bone, withdrawn a few millimeters, a small quantity of the drug mixture is delivered here. This procedure is repeated several times in different directions without removing the needle completely from its initial point of entry in the skin.^[9] The difference in injection technique may or may not affect the outcome of treatment with PRP in lateral epicondylitis. This study was conducted to compare whether there is any difference in outcome in terms of function and improvement in pain with the two techniques of injection.

MATERIALS AND METHODS

This prospective study was conducted among 62 patients who were diagnosed with lateral epicondylitis in the age group 18-65 years of both genders attending orthopaedic department at Malabar Medical College Hospital and Research Centre, Calicut, Kerala during July 2021 to July 2022.

Inclusion Criteria

Patients with pain more than 3 months and failed to respond to analgesic and physical therapy were included in the study. Patients of all genders were included. Patients aged between 18 and 65 years were included. Patients with clinically confirmed diagnosis of lateral epicondylitis were included.

Exclusion Criteria

Patients aged below 18 years and above 65 years were excluded. Patients with low hemoglobin concentrations (< 10 gm %) were excluded. Patients who had taken NSAIDs or any other analgesics within 3 days before injection were excluded. Patients who were on oral or injectable (local or systemic) corticosteroids were excluded. Patients with arthritis of elbow joint, calcifications around elbow or history of any fracture around elbow or bony abnormality or infection of the elbow joint were excluded. Patients who have undergone elbow surgeries, patients who had history of surgery for lateral epicondylitis, those who were having immuno-compromised status, those with history of

bleeding disorders, those on anticoagulants drugs intake, patients with alcohol and smoking habits, mentally challenged patients, were excluded from the study. All patients included were given the choice of joining the study. Ethical clearance was taken from ethical committee and informed consent was taken from all study participants.

Methodology

Patients were divided into two groups of 31 each. The first 31 patients (SI Group) were treated with PRP at the point of maximum tenderness at lateral epicondyle by single injection technique and the next 31 patients (PI Group) were treated with PRP at the point of maximum tenderness at lateral epicondyle by peppering injection technique. All the patients were blinded by type of injection. The PRP was prepared from venous whole blood of the patient using same method in both groups. PRP was prepared from 20 ml of venous blood collected in acid citrate dextrose anticoagulant vials. In its first centrifuge the collected venous blood was centrifuged for 10 minutes at 3000 rpm. A second centrifuge of separated plasma and buffy coat in separate plain tubes at 5000 rpm for final separation was done. Thus, obtained plasma solution contained 2/3 platelet poor plasma at the top and 1/3 platelet rich plasma at the bottom. The lower one-third plasma was drawn in sterile syringe and used for injecting into the anatomical point of maximum tenderness on lateral epicondyle. To activate the platelets in PRP before injection, calcium chloride was added to PRP in a 1:10 ratio. No delay was made after activating the PRP. No local anesthetic was used in both groups prior to injection of PRP.

Patient's demographic and occupational data were collected and patients were evaluated with pre injection assessment of Patient Rated Tennis Elbow Evaluation Score (PRTEE) and Visual analogue scale (VAS). No additional medications were given post procedure. Patients were advised to avoid lifting weights or heavy objects for 2 weeks and were advised to apply ice packs to the site of injection for two days. All the patients were followed up at the 2nd week, 4th week, 8th week and 12th week and assessed with PRTEE score and VAS score during each follow up.

Statistical analysis

For data entry Microsoft Excel 2013 was used. The Statistical Package for the Social Sciences (SPSS) version 24 software was used for all statistical calculations. Repeated measures of ANOVA was used to check statistical significance of both technique within both groups. Unpaired t test was used for comparison of results of two groups.

RESULTS

In total, 62 individuals participated in the study. 31 individuals in SI group and 31 individuals in PI group. The mean age of the overall study participants was 37.58±8.98 years. In SI group, the

mean age was 37.42 ± 9.10 years and in PI group, the mean age was 37.74 ± 9 years. The baseline

characters of the study participants were shown in [Table 1].

Table 1: Baseline characters of the study participants (n=62)

Characteristics	SI Group n (%)	PI Group n (%)	Overall n (%)
Gender			
Male	17 (54.8%)	15 (48.4%)	32 (51.6%)
Female	14 (45.2%)	16 (51.6%)	30 (48.4%)
Side involved			
Right	18 (58.1%)	22 (71%)	40 (64.5%)
Left	13 (41.9%)	9 (29%)	22 (35.5%)

The mean PRTEE score value at various follow-up for SI Group and PI Group patients is shown in [Table 2&3].

Table 2: Distribution of the study participants according to PRTEE score in SI Group (n=31)

Descriptive statistics	PRTEE Pre-procedure	PRTEE 2wk	PRTEE 4wk	PRTEE 8wk	PRTEE 12wk
Mean	77.081	71.79	38.242	22.29	10.097
Std. deviation	5.614	3.805	4.018	2.94	4.395
Minimum	67	62.5	33.5	16	0
Maximum	88.5	79.5	47.5	27.5	18

Table 3: Distribution of the study participants according to PRTEE score in PI Group (n=31)

Descriptive statistics	PRTEE Pre-procedure	PRTEE 2wk	PRTEE 4wk	PRTEE 8wk	PRTEE 12wk
Mean	77.29	55.016	27.258	16.919	1.468
Std. deviation	4.874	5.072	5.291	4.215	2.513
Minimum	68.5	40.5	20.5	10	0
Maximum	87.5	67.5	36.5	27.5	7.5

Repeated measures of ANOVA of PRTEE score was done for SI Group and PI Group separately and was found to be statistically significant ($p < 0.001$). There was improvement in functional outcome and pain in both SI and PI groups as per PRTEE scores calculated at regular interval.

The mean PRTEE scores of both SI group and PI group at regular follow up was compared. The mean score of PI group during 2nd week, 4th week, 8th week and 12th week follow up was better than SI group.

Comparison of PRTEE mean scores among SI Group and PI Group was done using unpaired t test. It is found that there is statistically significant difference in mean PRTEE score at 2 weeks, 4 weeks, 8 weeks and 12 weeks among SI Group and PI Group ($p < 0.001$). [Table 4]

Table 4: Comparison of PRTEE score among SI Group and PI Group (n=62)

	t value	p- value
PRTEE Pre-procedure SI Group vs PI Group	0.157	0.876
PRTEE 2wk SI Group vs PI Group	14.729	<0.001
PRTEE 4wk SI Group vs PI Group	9.204	<0.001
PRTEE 8wk SI Group vs PI Group	5.819	<0.001
PRTEE 12wk SI Group vs PI Group	9.488	<0.001

The mean VAS score value at various follow-up for SI Group and PI Group patients is shown in [Table 5 & 6].

Table 5: Distribution of the study participants according to VAS score in SI Group (n=31)

Descriptive statistics	VAS Pre-procedure	VAS 2wk	VAS 4wk	VAS 8wk	VAS 12wk
Mean	81.13	62.13	43.9	26.81	11.45
Std. deviation	7.056	10.164	8.076	5.069	4.932
Minimum	70	45	30	15	0
Maximum	91	75	55	33	21

Table 6: Distribution of the study participants according to VAS score in PI Group (n=31)

Descriptive statistics	VAS Pre-procedure	VAS 2wk	VAS 4wk	VAS 8wk	VAS 12wk
Mean	81.39	53.74	33.32	15.68	2.90
Std. deviation	8.007	10.761	6.925	3.449	4.036
Minimum	62	37	20	10	0
Maximum	95	66	46	25	10

Repeated measures of ANOVA of VAS score was done for SI Group and PI Group separately and was found to be statistically significant ($p < 0.001$). There was improvement in functional outcome and pain in both SI and PI groups as per VAS scores calculated at regular interval.

The mean VAS scores of both groups at regular follow up was compared. The mean score of PI group during 2nd week, 4th week, 8th week and 12th week follow up was better than SI group.

Comparison of VAS mean scores among SI Group and PI Group was done using unpaired t test. It is found that there is statistically significant difference in mean VAS score at 4 weeks, 8 weeks and 12 weeks among SI Group and PI Group ($p < 0.001$). [Table 7]

Table 7: Comparison of VAS score among SI Group and PI Group (n=62)

	t value	p- value
VAS Pre-procedure SI Group vs PI Group	0.135	0.893
VAS 2wk SI Group vs PI Group	3.155	0.003
VAS 4wk SI Group vs PI Group	5.537	<0.001
VAS 8wk SI Group vs PI Group	10.107	<0.001
VAS 12wk SI Group vs PI Group	7.468	<0.001

PRP injection treatment improved mean PRTEE score and mean VAS score during the 2nd week, 4th week, 8th week and 12th week in both single injection and peppering injection group showing improvement in functional outcome and pain with both injection technique. During follow up period the mean scores of PRTEE and VAS was better with peppering injection technique (PI Group) than single injection technique (SI Group). The final functional outcome and improvement in pain measured by both PRTEE score and VAS score at 12 weeks was better with peppering injection technique group which clearly establishes the superiority of peppering injection technique over single injection technique.

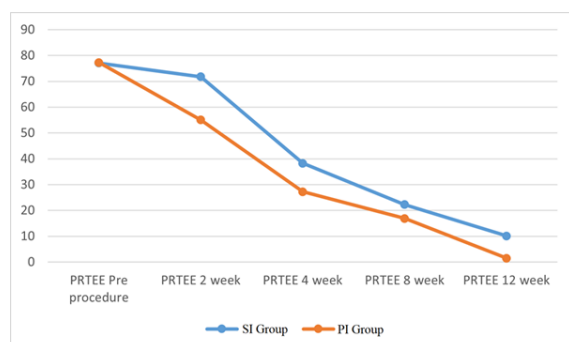


Figure 1: Comparison of mean PRTEE scores among SI Group and PI Group

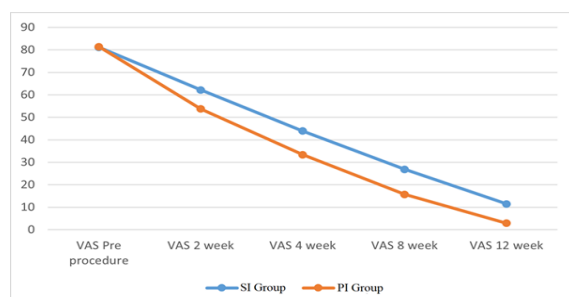


Figure 2: Comparison of mean VAS scores among SI Group and PI Group

DISCUSSION

The present study was a prospective study to compare the functional outcome and improvement

in pain following autologous platelet rich plasma treatment in lateral epicondylitis between single injection technique and peppering injection technique. Lateral epicondylitis is caused by repeated microtrauma to tendons at the bone tendon junction over lateral epicondyle especially Extensor carpi radialis brevis tendon.^[10] Many clinicians use the term “overuse syndrome” to define tennis elbow as an unpleasant pain resulting due to degeneration of the tendon caused by repetitive strain, overuse or poor biomechanics.^[11] It also affects the quality of life by affecting the capacity to use the joint in both personal and occupational day to day activities.^[12]

Autologous PRP injection therapy is nowadays used in treatment of tennis elbow and is very effective in treating the condition.^[2,13,14] Various injection treatment with local steroid infiltration (40 mg of triamcinolone) into the afflicted tendon sheath, as well as local sodium hyaluronate injection has been tried for lateral epicondylitis.^[15,16] Homologous platelet lysate (HPL) injection, autologous tenocytes injection, autologous blood injections and tissue bioengineering with mesenchymal stem cells and silk scaffolds are all being investigated.^[17,18]

In the present study, the mean age overall study participants was 37.58 ± 8.98 . There were 32 (51.6%) males and 30 (48.4%) females. In 40 (64.5%) patients the right elbow was involved and in 22 (35.5%) patients left elbow was involved.

In the present study, repeated measures of ANOVA of PRTEE score and VAS score was done for SI Group and PI Group separately and was found to be statistically significant ($p < 0.001$). There was improvement in functional outcome and pain in both SI and PI groups as per PRTEE scores and VAS scores calculated at regular interval. Thus, PRP was effective in improving functional outcome and pain by both single injection technique and peppering injection technique. The preprocedural mean PRTEE and mean VAS score was comparable in both SI group and PI group. During follow up at 2 weeks, 4 weeks, 8 weeks and 12 weeks the mean PRTEE score and mean VAS score was better in PI group when compared to SI group. Comparison of PRTEE mean scores and VAS mean scores among

SI group and PI group was done using unpaired t test. It is found that there is statistically significant difference in mean PRTEE and mean VAS scores during regular follow up interval among SI group and PI group ($p < 0.001$). Hence the main finding in our study was that peppering technique (PI group) was effective than single injection technique (SI group) in the treatment of lateral epicondylitis, with injection of platelet rich plasma. The final mean scores of PRTEE and VAS score at 12 weeks was better with peppering injection technique when compared with single injection technique.

Prakash et al, conducted a prospective randomized study comprising of 25 patients in each group (single versus peppering injection group) with the aim to compare the results of injecting steroid and lignocaine mixture via single injection and peppering injection technique. They found that the mean PRTEE score was 22.36, 18.40 and 14.16 at 2 weeks, 6 weeks and 6 months following peppered injection as compared to 28.96, 21.84 and 25.32 in the single injection group (p value < 0.05). VAS score at 2 weeks, 6 weeks and 6 months after the peppered injection was found to be 2.72, 1.72 and 1.36 and in the single injection group was 2.96, 1.92 and 2.72 at 2 weeks, 6 weeks and 6 months, respectively (p value < 0.05). On comparison of the 2 groups, there was a significant reduction of VAS scores at 6 months post-injection (p value < 0.05) and PRTEE score at 6 weeks, 6 months in peppered injection group. Their study concluded that the effects of peppered injection technique is advantageous over the single injection technique in the management of chronic lateral epicondylitis.^[19]

Okcu et al, compared the efficacy of single injection and peppering injection techniques of local corticosteroid and local anesthetic in the management of lateral epicondylitis. Patients were evaluated with the Turkish version of the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire before injection and at the final follow-up and found that The Turkish DASH scores of peppering injection group were significantly lower than those of single injection group ($p=0.017$). They concluded that the peppering technique appears to be more effective than the single injection technique in the long-term.^[20]

Gaspar et al, conducted a cohort study with a total of 93 patients with recalcitrant lateral epicondylitis who were treated with PRP injection by percutaneous needle fenestration ($n = 45$) or percutaneous needle tenotomy ($n = 48$) over a 5-year study interval. At a mean follow-up of 40 months, significant improvements in VAS, Quick DASH and PRTEE scores and grip strength were observed across the entire study cohort, with no significant differences noted between the fenestration and tenotomy groups.^[21]

Goorens et al, conducted a prospective study which describes the results of the short-term follow-up of 56 patients with treated with the Instant Tennis Elbow Cure Medical device, which fenestrates the

injured tendon in a standardized way through a holder of 12 small needles through which Unprepared autologous blood was injected in the tendon. Visual analog pain scale (VAS) decreased significantly in rest by 61% and during activity by 47% after 6 weeks. VAS decreased significantly in rest by 79% and during activity by 66% after 3 months. VAS did not remain significantly different after 6 months.^[22]

The mechanism of action of peppering injection technique is attributed to a more even distribution of PRP around the diseased tendon site where as single injection technique delivers the PRP to a single point only. Peppering injection technique causes local bleeding and hematoma formation by multiple injections (peppering) through the granulation tissue and degenerating tendons. The hematoma formation and bleeding further increase concentration of the growth factors already present in PRP. This bleeding and local hematoma formation thus starts healing process of the area of tendinosis.^[20,23] Peppering causes mechanical disruptions over the tendinosis site. The mechanical disruption caused by peppering injection may transform a failed intrinsic healing process into an extrinsic response.^[9,24]

CONCLUSION

Platelet rich plasma is now widely used for the treatment of Lateral epicondylitis and it has shown good results in the long term without any tendon degeneration. Single injection of PRP is effective in improving functional outcome and decreasing pain by inducing healing in the injured tendon as shown by the results analyzed. Better healing was induced by peppering injection technique. Also, the functional outcome and improvement in pain was better with peppering injection technique than with single injection technique. Peppering injection technique caused more even distribution of PRP, local bleeding and hematoma formation by multiple injections (peppering) through the granulation tissue and affected tendons. This can cause faster healing process of the injured tendon. So, whenever PRP is used in treatment of lateral epicondylitis, peppering injection technique may be preferred over single injection technique for better functional outcome and improvement in pain.

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