

Randomized Controlled Trial of Intra-Lesional Injection of Platelet Rich Plasma V/S Intra- Lesional Triamcinolone Acetonide In The Management of Lateral Epicondylitis

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Abstract: Tennis elbow is the most common cause of elbow pain in patients attending the orthopaedic clinics. Pathophysiology involves micro tears in the tendon leading to haemorrhage, rough granulation tissue formation and later repair. . Even though the different treatment modalities of tennis elbow have been claimed to be effective in treating this condition due to its chronic nature and tendency to recur with resumption of activity, no single modality has been considered. Platelet-rich plasma prolotherapy (PRPP) is an injection treatment that has been used in recent times for various enthesopathies. It repairs incompletely healed injuries thereby reducing pain and increasing function. Our study aims to compare the efficacy of PRPP and compare it with the more traditionally used steroid in the population of this part of the country. This based randomized, prospective, interventional study was conducted on patients of lateral epicondylitis visiting our OPD. A total of 200 patients were included in the study. Improvement in the PRP injection group was significantly greater than that in the corticosteroid injection group ($P < 0.001$).

From this study it was concluded that both local corticosteroid and PRP injection therapy are simple outdoor procedures for the treatment of lateral epicondylitis. However, PRP is better in terms of long term relief and very negligible side effects.

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I. Introduction

Tennis elbow is the most common cause of elbow pain in patients attending the orthopaedic clinics¹. Although it has been commonly termed tennis elbow, it is seen to affect non sports personnel more in comparison to the sports. It occurs most commonly in the tendon of extensor carpi radialis brevis. Pathophysiology involves microtears in the tendon leading to haemorrhage, rough granulation tissue formation and later repair. Overuse from many activities, including sports, result in this disorder². The constellation of findings has been termed as angiofibroblastic hyperplasia³. Platelet-rich plasma prolotherapy (PRPP) is an injection treatment that stimulates healing⁴. It repairs incompletely healed injuries thereby reducing pain and increasing function⁴. Platelet-rich plasma prolotherapy (PRPP) involves the injection of autologous blood, in particular the portion concentrated with platelets, into the donor's body at the site of concern⁴. It is known to increase growth factor concentration 3-5 times to that of normal plasma and helps to accelerate healing of the injured tissue^{5, 6}. Since PRPP uses autologous blood, chances of immunogenic reactions or disease transfer that may occur from the usage of non-autologous blood are negated. This study was undertaken to compare the Efficacy of intra-lesional injection of platelet rich plasma V/S intra-lesional Triamcinolone acetonide in the management of lateral epicondylitis with a 3 month follow up.

II. Materials and methods

This hospital based randomized, prospective, interventional study was conducted on an OPD basis in the Department of Orthopaedics, Gauhati Medical College And Hospital, Guwahati. The study was conducted over a period of 15 months, from 1st June 2017 to 31st August 2018 after getting clearance from the Ethical Committee of the Institute.

Study Design: Randomized, prospective, interventional study.

Study Location: This was a tertiary care teaching hospital based study done in Department of Orthopaedics, Gauhati Medical College and Hospital, Bhangagarh, Guwahati, Assam, India.

Study Duration: 15 months, from 1st June 2017 to 31st August 2018.

Sample Size: 200 Patients.

Sample Size Calculation: the sample size was calculated on the basis of single proportion design. The target population from which we randomly selected our sample was considered 20000. We assumed that the confidence interval of 10% and confidence level of 95%. The sample size obtained was 96 patients for each group. We included 100 patients in each group with 4% drop out rate.

Subjects and selection method: Patients with chronic elbow pain who came to the OPD were evaluated through proper history taking and clinical examination according to the set proforma. The patients having following criteria were included in this study:

Inclusion Criteria:

- History of pain at lateral aspect of elbow more on lifting weights, grasping and twisting activities.
- Pain over lateral epicondyle of at least 15 days duration.
- Positive Cozen's Test.
- Age 20 -50 years.
- Either sex.

Exclusion criteria:

- Pregnancy.
- History of trauma.
- Hyperglycemia.
- Low blood pressure; hemodynamic instability.
- Dysfunctional platelets and clotting (hemophiliacs).
- Consistent use of NSAIDs (anti-inflammatory drugs) within 48hours of PRP procedure.
- Corticosteroid injection at treatment site within two weeks of PRP procedure.
- Corticosteroid orally or IV within two weeks of PRP.
- Rash at injection site.
- Other causes that mimic Tennis Elbow e.g. Osteochondritis-dessicans of Capitellum, Epiphyseal Injury, Varus instability, Radial head arthritis, Posterior Interossious nerve syndrome, Cervical disc lesions, Radio Humeral joint synovitis, Fibromyelgia.

Procedure methodology:

Patients were counseled about the procedure and after informed and written consent, standard proforma was filled. Patients were divided in two groups based on computer based randomization chart. 100 patients (n=100) in each group were taken.

Group 1 received intra-lesional injection of platelet rich plasma (1-2ml).

Group 2 received intra-lesional injection of Triamcinolone acetonide (1 ml).

Group 1 (PRP group): n = 100.

Group 2 (Triamcinolone group): n = 100.

For those in group 1, 10 ml of whole blood was withdrawn from the patient from the contralateral elbow and 1ml of PRP was prepared using differential centrifugation technique with two spins using SYMAX Centrifuge machine, India. Blood was collected in Sodium heparin vacuum vials. The 1st spin was performed at 1500 rpm for 15 minutes. This spin separated the red blood cells from rest of the components. The upper half of the supernatant was discarded and the lower half was transferred to another plain vial and spinned at 2500 rpm for 10 minutes. The lower half of the supernatant was taken in a 1ml syringe. At the end of preparation the samples were sent for platelet count and compared with patients count. After proper positioning of the patient (flexion of the elbow either in lying or sitting position, bony landmarks identified), under all aseptic and antiseptic precautions, a 22G hypodermic needle was inserted into the affected elbow 5mm distal to the lateral epicondyle in the extensor tendons, particularly the extensor carpi radialis brevis tendon and PRP was administered using peppering method. As autologous blood transfusion is being done there is no need of any cross matching or blood grouping.

For those in group 2, Inj. Triamcinolone acetonide 1ml. was administered using previous mentioned method. Patients were advised to rest the upper limb for three days, with no restriction of activity after that. Paracetamol 650mg was advised on an SOS basis following injection. Patients were assessed using the two following scores before and after treatment at 2 weeks, 6 weeks, and 3 months.

- Visual analogue scale (VAS) for pain,
- Disabilities of the Arm, Shoulder and Hand Scale (DASH) score for functional evaluation.

Statistical analysis:

Data was analyzed using MedCalc statistical software version 19.0.5. Student's t-test was used to ascertain the significance of differences between mean values of two continuous variables and confirmed by nonparametric Mann-Whitney test. In addition, paired t-test was used to determine the difference between baseline and at 2 weeks and 3 months regarding VAS and DASH scores, and this was confirmed by the ANOVA test which is a nonparametric test that compares two paired groups. Chi-square test and Fisher test were performed to test for differences in proportions of categorical variables between two groups. The level $P < 0.05$ was considered the cut off value or significant.



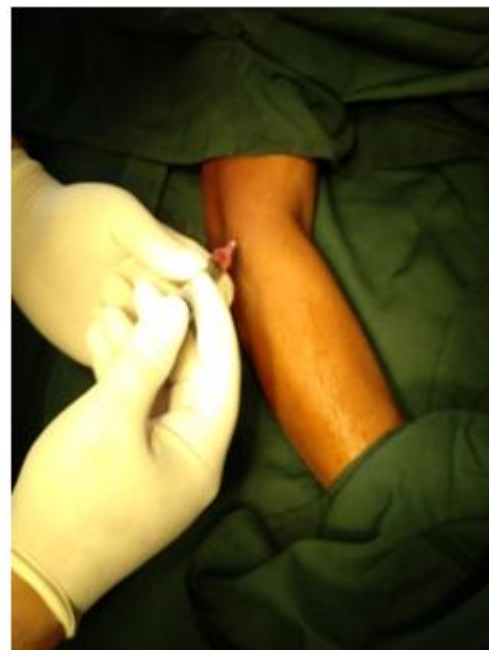
SODIUM HEPARIN VACUUM VIAL



AFTER 1ST SPIN



PREPARED PRP AFTER 2ND SPIN



ADMINISTRATION OF PRP INJECTION

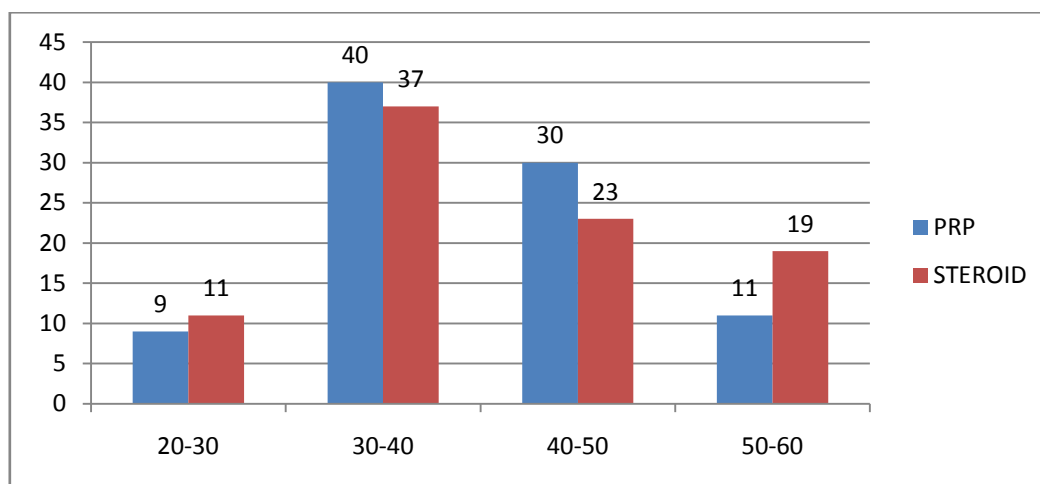
III. Results

We enrolled 200 adult patients of either sex having lateral epicondylitis, coming to the Orthopaedics OPD, Gauhati Medical College and Hospital, Guwahati. After randomization the intervention in the form of either PRP or Triamcinolone Acetonide Injection was given. 10 patients in PRP group and 14 in Steroid group were lost in follow up and therefore not included in evaluation of results. 176 adult patients of either sex affected by lateral epicondylitis (tennis elbow) were enrolled in the study and they were divided into two groups of 90 patients in one group and 86 in the other. Group A patients were given PRP injection at the site of maximum tenderness over the lateral epicondyle of the humerus. Single dose of PRP injection was given. Group B patients received local Triamcinolone acetamide injection at the point of maximum tenderness over the lateral epicondyle of the humerus.

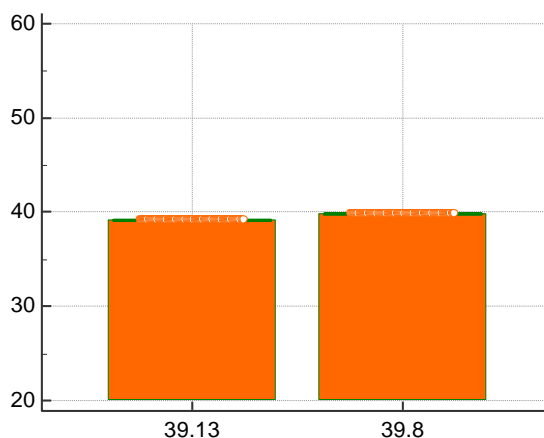
Comparison of age groups in the two study groups is not significant (computed using Students t-test assuming equal variances, since F-test for equal variances succeeded [$p=0.6245$]). Hence, two groups have similar age distribution and are comparable to each other. The mean age in Group 1 and group 2 are 39.13 and 39.8 respectively (Table 2, Graph 1 &2)

Table 1: Summary statistics comparing the age distribution of 2 groups

	Group 1 (PRP)	Group 2 (STEROID)
Sample size	90	86
Arithmetic mean	39.13	39.8
95% CI for the mean	37.43- 40.83	37.69- 41.94
Variance	66.13	98
Standard deviation	8.132	9.94
Standard error of the mean	0.8573	1.072
Significance	P=0.6245*	

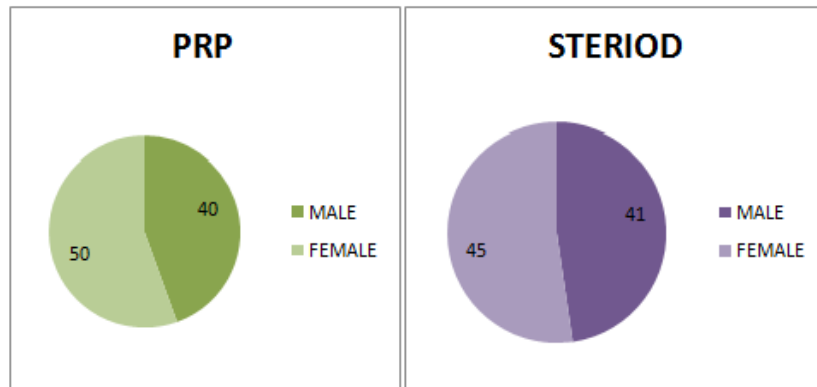


Graph 1: Bar diagram showing age distribution between two groups



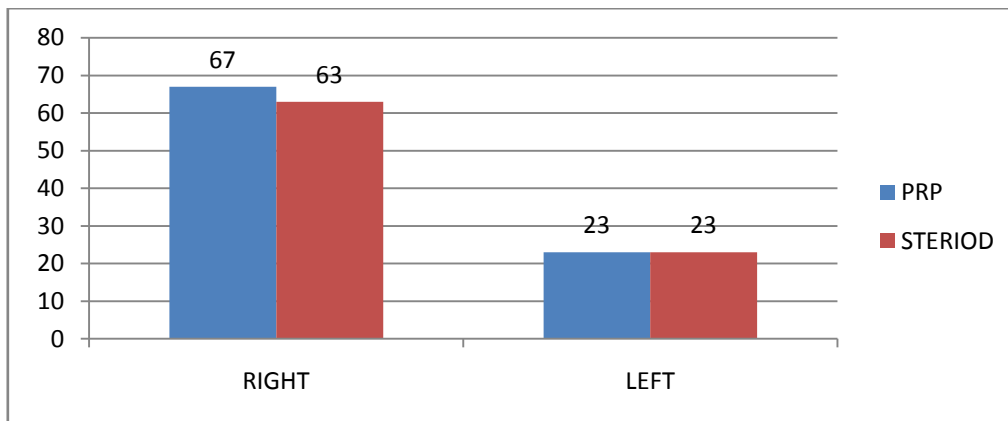
Graph 2: Comparison of mean age between the 2 groups.

There were 51% male and 48% female patients with the age group varying from 21 to 60 years and an average age of the patients was 39 years. (Graph 3, Table 3)



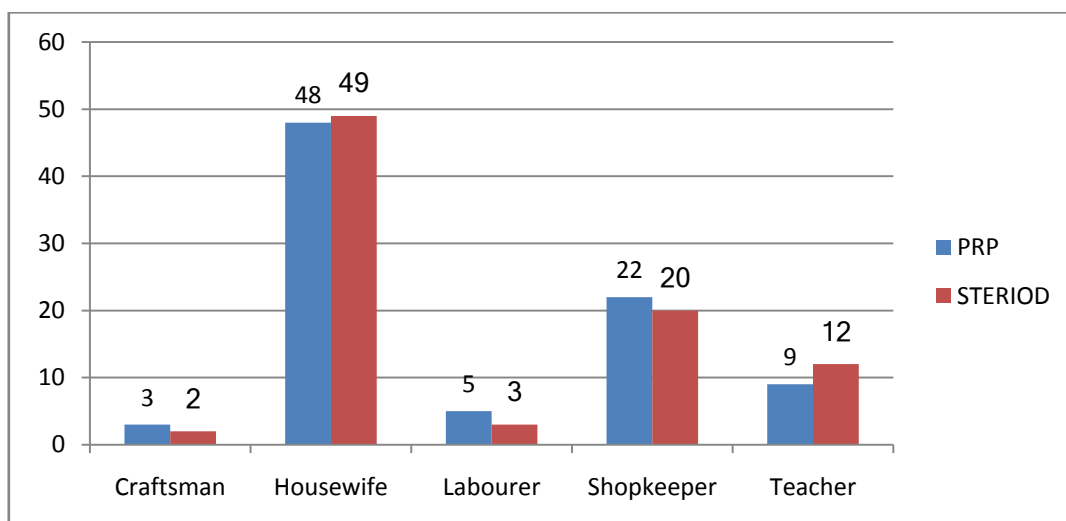
Graph 3: Pie diagram showing gender distribution of 2 groups

Amongst 176 enrolled patients, 130 (73.86%) showed involvement of right elbow and 46(26.1%) showed involvement of left side. All showed their dominant side to be affected.



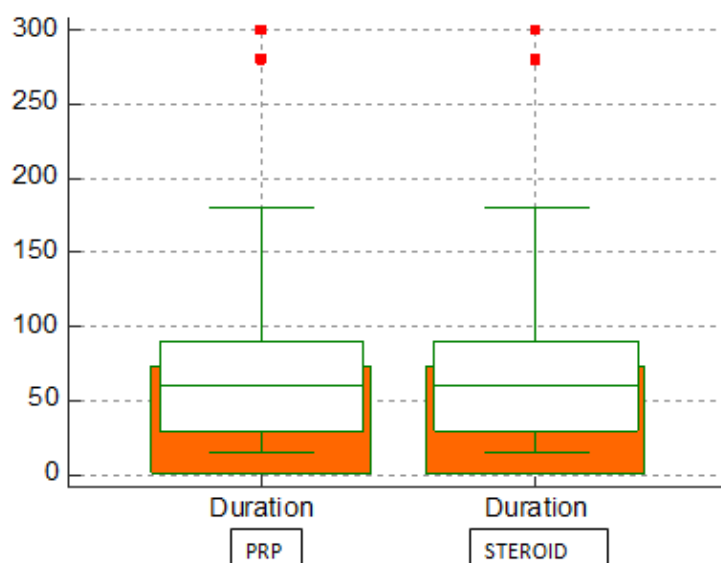
Graph 4: Showing distribution of affected side among 2 groups

In our study, 55.11% cases were housewives, 4.5% were labourers, 11.93% teachers, 23.86% shopkeeper and 2.84% craftsmen, and thus showing that lateral epicondylitis is common in persons involved in repeated rotational movements of the forearm. It was also seen in our study that majority of female patients (55.11%) were housewives involved in routine household activities like dusting, brooming, sweeping, washing clothes and utensils. (Graph 5)



Graph 5: Showing distribution of occupation among 2 groups

The average duration of pain at the time of presentation was 70 Days. In the PRP group lowest duration of symptom was 18days and maximum duration was 360days. In the Steroid group lowest duration of symptom was 15 days and maximum duration was 300 days. (Graph 6)



Graph 6: Comparison of mean duration of symptoms in both the groups.

The results were evaluated using two scoring systems the VAS and DASH scores. Both VAS and DASH scores were taken at presentation and later after giving injections at 2weeks, 6weeks, and 3 months. The pre-procedure and post procedure VAS and DASH scores were compared.

The mean VAS and DASH scores were compared using ANOVA test and the results are as follows (Table 6, Table 7)-

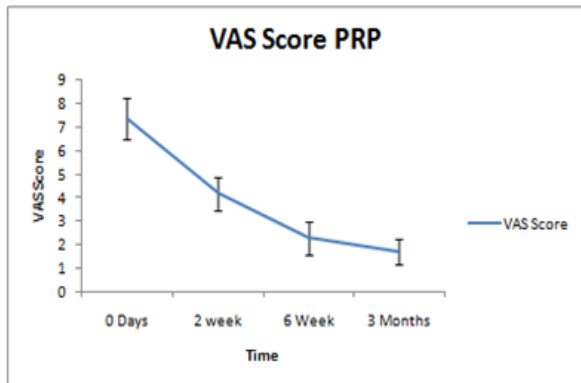
Table 6: Comparison of VAS & DASH score at different intervals in PRP group

Group	Time	Mean ± S.D	P-Value	Remark
VAS Score	0 Days	7.36 ±.891	<0.001	Significant
	2 week	4.19 ±.701		
	6 Week	2.28 ±.701		
	3 Months	1.70 ±.529		
DASH Score	0 Days	61.092 ± 7.5498	<0.001	Significant
	2 week	42.870 ± 7.7744		
	6 Week	16.448 ± 4.7057		
	3 Months	9.679 ± 5.2082		

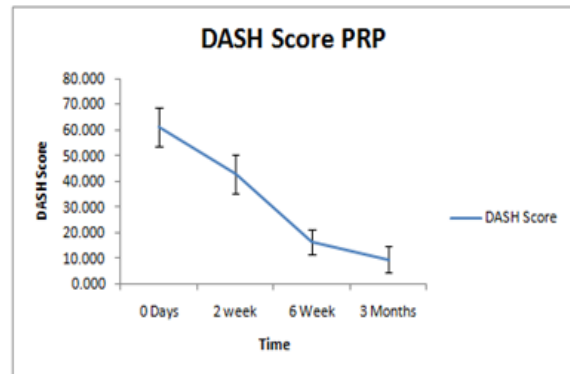
Table 7: Comparison of VAS & DASH score at different intervals in steroid group

Steroid	Time	Mean ± S.D	P-Value	Remark
VAS Score	0 Days	6.98 ± 1.051	<0.001	Significant
	2 week	5.48± 0.991		
	6 Week	3.50±1.026		
	3 Months	2.93±0.892		
DASH Score	0 Days	60.708 ±7.04	<0.001	Significant
	2 week	45.638±8.28		
	6 Week	26.873 ± 8.16		
	3 Months	18.694±4.67		

We observed a significantly higher short-term success rate with corticosteroid injection compared with PRP injection. At 2 weeks the mean reduction of VAS score in PRP group was 3.17 (from 7.36 to 4.19). At 2 weeks the mean reduction of VAS score in steroid group was 1.5 (from 6.98 to 5.48). However the DASH score was comparable in both the groups at 2 weeks.

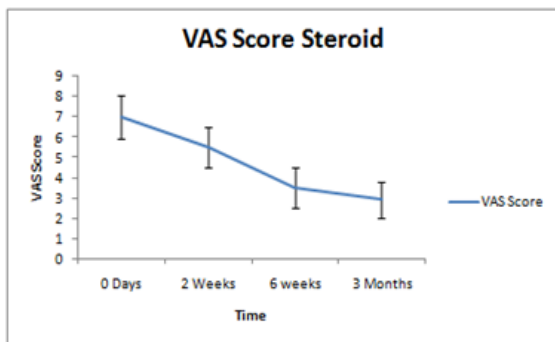


Graph 7: VAS score at subsequent follow-up.

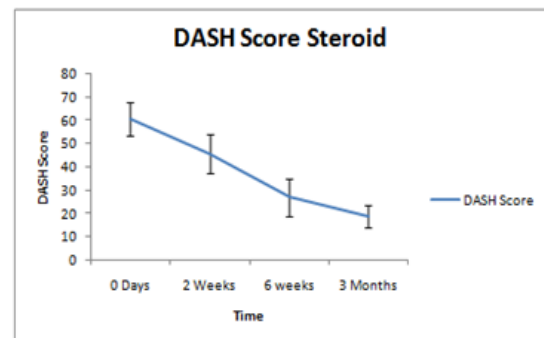


Graph 8: DASH score at subsequent follow-up.

At 3 months follow-up the mean reduction in VAS value was 5.66 (from 7.36 to 1.70; 76%) in the PRP injection group and 4.05 (from 6.98 to 2.93; 58%) in the corticosteroid injection group.

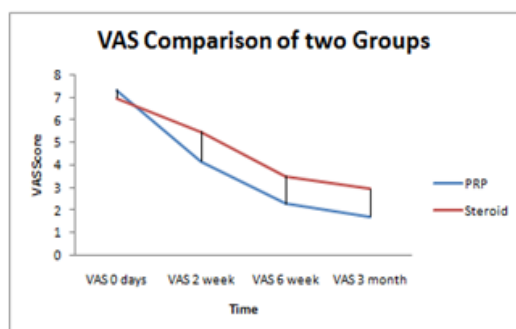


Graph 9: VAS score at subsequent follow-up.

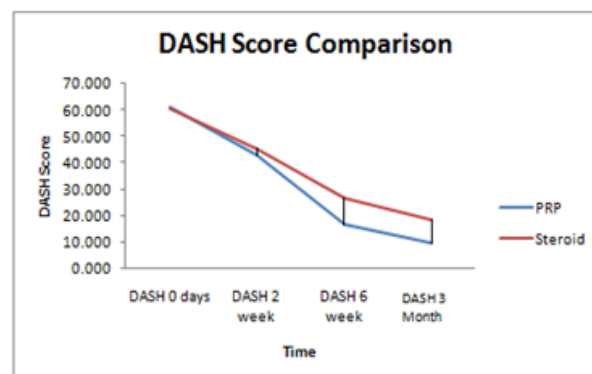


Graph 10: DASH score at subsequent follow-up

The mean reduction in VAS and DASH scores between the PRP and Steroid groups was compared using Mann whitney U test and the graph was plotted.(Graph 11,12)



Graph 11: Comparison of Mean reduction of VAS scores



Graph 12: Comparison of Mean reduction of DASH scores

Improvement in the PRP injection group was significantly greater than that in the corticosteroid injection group (P<0.001).

IV. Discussion

Corticosteroid injection is often used in the treatment of lateral epicondylitis. Although the effects of corticosteroid injection are not fully known, they are thought to be related to the haemorrhage resulting from the high-pressure, forced injection in the tissue planes.⁷ Corticosteroids have various effects on cells, and presumably their ability to limit intracellular activity by reducing the nuclear-cytoplasmic communication pathways influences the degenerative and reparative components of this condition.⁸ Many different results have

been reported with corticosteroid injection. Some studies have described a high success rate in the short term with corticosteroid injection^{9, 10, and 11,12}. In these studies, corticosteroid injection was compared with NSAIDs, physical therapy, elbow band, splintage, and wait-and-see approaches; the early results were successful with corticosteroid injection^{11, 13, 14,15}. In our study, we also observed a significantly higher short-term success rate with corticosteroid injection compared with PRP injection. At 2 weeks the mean reduction of VAS score in PRP group was 3.17 (from 7.36 to 4.19). At 2 weeks the mean reduction of VAS score in steroid group was 1.5 (from 6.98 to 5.48). However the DASH score was comparable in both the groups at 2 weeks.

Assendelft et al,⁹ in their 1996 systematic review, compared the validity and outcome of randomised controlled trials of corticosteroid injections for lateral epicondylitis. Pooled analysis indicated short-term effectiveness only (two to six weeks). At follow-up of more than six weeks, no difference was found between corticosteroid injection and other treatments, including placebo. In our study on comparing the VAS and DASH scores at 3 months better reduction has been found in the PRP group(P<0.001)

Recent reports have emerged suggesting a beneficial role of growth factors delivered locally at the site of tendinopathy. This can be accomplished by injection of PRP.

Mishra and colleagues¹⁶ conducted a study wherein they treated patients of lateral elbow tendinopathy of less than 6 weeks duration by local injection of platelet rich plasma. They reported a significant improvement in pain.

Similarly Edwards et al.¹⁷ reported dramatic relief in symptoms in 28 patients of tennis elbow after injection of PRP. They postulated that PRP initiated an inflammatory reaction which allowed healing in the otherwise degenerative process.

At 3 months follow-up the mean reduction in VAS value was 5.66 (from 7.36 to 1.70; 76%) in the PRP injection group and 4.05 (from 6.98 to 2.93; 58%) in the corticosteroid injection group.

The mean improvement in PRP injection was significantly more than that in the corticosteroid group. (P<0.001)

The mean improvement in DASH score in PRP injection group and corticosteroid injection group were 51.41(from 61.09 to 9.67; 83%) and 42.01 (from 60.70 to 18.69; 37.70%) respectively.

Improvement in the PRP injection group was significantly greater than that in the corticosteroid injection group. (P<0.001)

Injection therapies have the risks of post-injection flare, iatrogenic infection, tissue atrophy, fat necrosis, tendon rupture, nerve damage etc. In our study we did not encounter any severe side-effects in both the groups. However, one patient developed local depigmentation at injection site in the steroid group.



Fig 1 : Local depigmentation after steroid injection.

V. Conclusion

The results analysed at 2 weeks, 6 weeks and 3 months, showed significantly better results in patients who were given PRP injection which was supported by the evidence of literature.

From this study it is concluded that both local corticosteroid and PRP injection therapy are simple outdoor procedures for the treatment of lateral epicondylitis. Due to better long-term results in PRP injection and high recurrence rate in steroid injection, we suggest that the treatment of choice for lateral epicondylitis be PRP injection therapy.

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