

Comparative outcomes of platelet rich plasma, autologous blood and corticosteroid injections in the treatment of lateral epicondylitis

Huseyin Gokhan Karahan¹, Recep Selcuk Eyceyurt², Levent Kucuk³, Huseyin Gunay³, Erhan Coskunol³

ABSTRACT

Objectives: Lateral epicondylitis is a disorder in which the dominant extremity is usually affected, and its prevalence ranges between 1% and 3% in the general population. It appears to be more common and severe in women between ages 30 and 60. Platelet rich plasma (PRP), autologous blood and corticosteroid injections are widely applied treatment modalities with various success rates. We aimed to investigate clinical outcomes of these three injection techniques. Study Design is Prospective randomized clinical trial.

Methods: Fifty two patients (19 men, 33 women) whom were diagnosed lateral epicondylitis between the years 2011 and 2013, with a mean age 43,7years (min 18, max 62) were randomized into three groups according to application order. Each group received one of the injection treatments: PRP, autologous blood or corticosteroid. Comparative clinical outcomes evaluated prospectively. Assessments performed by a blind evaluator by visual analog scale (VAS), presence of tenderness, QuickDASH scores, grip strength measurements in pre-injection period and in post-injection first, third and sixth months. Statistical analyses performed in SPSS 21 software by Pearson's chi-squared, Anova, Kruskal Wallis and McNemar tests.

Results: Changes of VAS and QuickDASH scores in each group were significant according to pre-injection and post-injection first, third, sixth month evaluations ($p<0,001$). There were significant changes in autologous blood ($p=0,016$) and PRP ($p=0,008$) groups in presence of tenderness among post-injection first and sixth month controls.

Conclusions: Significant improvement obtained in all three groups both in early and late post-injection periods. With respect to subjective outcomes, the most obvious improvement noticed in platelet rich plasma group especially in late period.

Key words: Autolog blood, corticosteroid, epicondylitis, PRP

Introduction

Lateral epicondylitis is a disorder in which the dominant extremity is usually affected, and its prevalence ranges between 1% and 3% in the general pop-

ulation. It appears to be more common and severe in women between ages 30 and 60 [1,2].

The primary cause of lateral epicondylitis is repetitive overloading of the muscle-tendon unit, which

Author affiliations : Department of Orthopaedics and Traumatology, ¹Bozyaka Surgery Research and Training Hospital, Izmir, ²Oltu State Hospital, Erzurum, ³Ege University, Izmir, Turkey

Correspondence : Recep Selcuk Eyceyurt, MD, Department of Orthopaedics and Traumatology, Oltu State Hospital, Erzurum, Turkey
e-mail: reyceyurt@gmail.com

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causes fatigue-related ruptures and results in healing problems if it persists. Lateral epicondylitis is classified as a disability by the World Health Organization, since it frequently limits work capacity. It is also a common reason for retirement.

There are a number of modalities for the treatment of lateral epicondylitis [3,4]; however, no consensus has been reached regarding a gold standard modality for the treatment of this disorder [5].

In the planning phase of this study, we took into consideration the efficacy of conservative treatment modalities for tennis elbow in the chronic period; this disorder has a tendency to become chronic, resulting in permanent workforce loss in the population. In this prospective, randomized, controlled, blinded study, early and late-term effects of single-dose steroid (SE), autologous blood (AB) and platelet-rich plasma (PRP) injections for the treatment of chronic tennis elbow were evaluated.

Materials and Methods

A total of 52 patients who had received an initial diagnosis of lateral epicondylitis were randomized into three groups, and their treatment responses were prospectively analyzed. Nineteen (36.5%) were males and 33 (63.5%) females, with ages ranging between 18 and 62.

The inclusion criteria included a minimum score of 50 on the visual analog scale (VAS), tenderness on the lateral epicondyle (a positive direct palpation test), pain with resistant wrist extension, the use of NSAID drugs, the use of elbow splints, the previous receipt of physical therapy with no relief of symptoms within the last three months, and ongoing pain at rest.

Patients who had received local injections at the site of tenderness were excluded from the study. An informed consent form was obtained from each patient.

The patients randomized into groups received one of three injectants, AB, PRP and SE, at the site of tenderness over the lateral epicondyle.

Group 1 patients (n=17): 2 ml of AB obtained

from the healthy arm was administered to the local site of tenderness at the epicondyle after the injection of 1 ml of prilocaine.

Group 2 patients (n=18): 25 ml of blood obtained from the healthy arm and 5 ml of calcium citrate were transferred to the Prosys PRS Bio Kit (20 kits were purchased by the University Scientific Research Projects Committee). The buffy coat and plasma were separated, and the buffy coat was placed into the middle layer of the PRP kit (syringe guide). It was then drawn into the syringe and mixed with the plasma, and 2 ml of platelet-rich plasma was obtained. The PRP was then applied to the local site of tenderness at the epicondyle after the injection of 1 ml of prilocaine.

Group 3 patients (n=17). Celestone® Chronodose 1 ml suspension (containing 3 mg of betamethasone acetate and 3.947 mg betamethasone disodium phosphate) was mixed with 1 ml of normal saline, and a 2 ml solution was obtained. SE was administered to the local site of tenderness at the lateral epicondyle after the injection of 1 ml of prilocaine.

Following the injection, each patient was placed in a long-arm cast brace, which was removed one week later. Within two weeks after the removal of the braces, three sets of stretching exercises four times a day were initiated for each patient, followed by elbow flexion, extension, supination and pronation exercises.

The patients were invited for follow-up at the end of months 1, 3 and 6. The site of local tenderness, bilateral grip strength, VAS and Quick DASH scores were analyzed by a separate blinded orthopaedic surgeon who had also performed the preoperative evaluation, and the results were recorded.

Data were analyzed using the SPSS 21 program, using the Pearson chi square (Monte Carlo), ANOVA, Kruskal Wallis and McNemar tests.

Results

The mean age of the patients was 43.7 ± 9.9 years ($p=0.310$). The study included 19 males (36.5%) and 33 females (63.5%) ($p=0.629$). The randomization ac-

Table 1. Statistical evaluation of Quick DASH scores between groups.

	GROUPS			P value
	AB=A	PRP=B	Steroid=C	
QuickDash Preoperative	53,5±16,4	57,4±13,0	44,6±15,8	
QuickDash 1. month	31,2±17,6	33,8±13,6	28,5±17,9	
Changed QuickDash (Preoperative - 1. month)	22,2±22,5	23,6±20,3	16,1±16,0	0,497
QuickDash 3. month	20,0±18,2	17,2±13,3	22,5±16,6	
Changed QuickDash (Preoperative - 3. month)	33,5±21,7	40,3±20,8	22,0±18,7	0,036
	P(A-B)=0,331	P(A-C)=0,108	P(B-C)=0,011	
QuickDash 6.month	12,9±16,6	9,8±9,8	20,8±18,4	0,003
Changed QuickDash (Preoperative - 6. month)	40,6±22,2	47,6±16,5	23,8±20,4	
	P(A-B)=0,301	P(A-C)=0,017	P(B-C)=0,001	
**P value	<0,001	<0,001	<0,001	
General Linear Model RepeatedAnova (Wilks' Lambda - Huynh-Feldt) **P value: Change for QuickDash in groups				

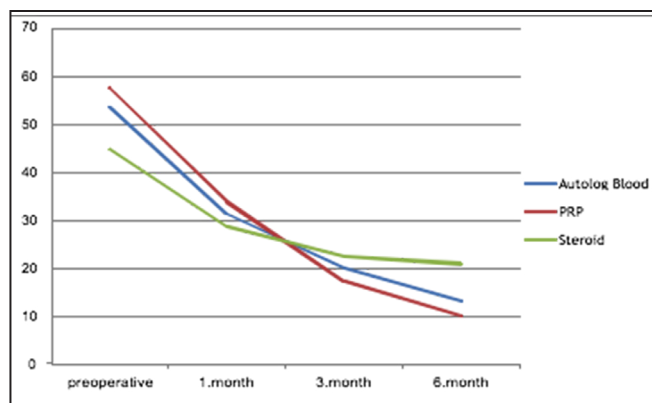


Figure 1. Recovery of Quick-DASH scores in the first month evaluation can be noticed in all groups. While PRP and autologous blood groups still have diminished scores in the sixth month, increase in Q-DASH scores was noticed in CS group.

cording to age and gender revealed no significant difference between the groups ($p < 0.05$).

The AB and SE groups included 17 patients each and the PRP group 18 patients. The right arm was affected in 75% ($n=39$) of patients, and the left arm in 25% ($n=13$) of patients. The randomization of the affected extremity was not statistically significant between the groups ($p=0.619$). The mean duration of patients' complaints was 9.13 ± 6.2 months.

The comparison of Quick DASH symptom scores preoperatively and at a six-month follow-up revealed a significant difference between the three groups

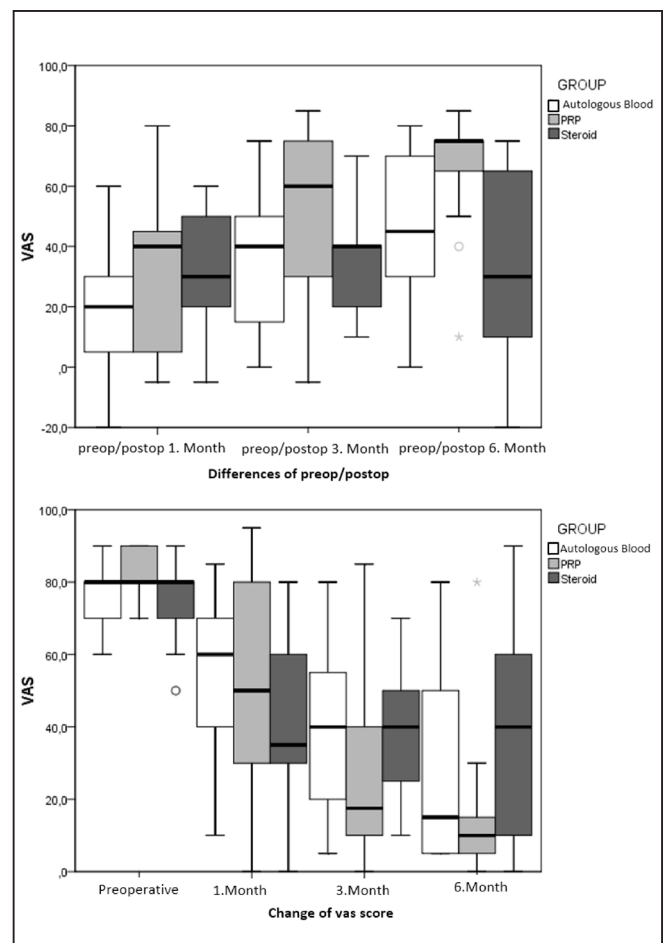


Figure 2. The greatest decrease in VAS score was noticed in CS group in the first month evaluation. But CS group did not able to keep this recovery in long term. PRP group has got significantly better results among the other groups according to VAS scores.

Table 2. Statistical evaluation of pain evaluation according to visual analog scale(VAS) Table 3: Inter and intra group statistical evaluation of grip strengths.

	GROUPS			*P value
	AB=A	PRP=B	Steroid=C	
VAS Preoperative	*80,0±10,0	*80,0±10,0	*80,0±10,0	
VAS 1. month	*60,0±30,0	*50,0±50,0	*35,0±30,0	
Changed Vas (Preoperative1.month)	*20,0±25,0	*40,0±40,0	*30,0±30,0	0,357
VAS 3. month	*40,0±35,0	*17,5±30,0	*40,0±25,0	
Changed Vas (Preoperative3. month)	*40,0±35,0	*60,0±45,0	*40,0±20,0	0,048
	P(A-B)=0,030	P(A-C)=0,923	P(B-C)=0,038	
VAS 6. month	*15,0±45,0	*10,0±10,0	*40,0±50,0	
Changed Vas (Preoperative6. month)	*45,0±40,0	*75,0±10,0	*30,0±55,0	0,001
	P(A-B)=0,026	P(A-C)=0,342	P(B-C)=0,001	
**P value	<0,001	<0,001	<0,001	
***P value for AB	P(Preop-1.month)=0,201 P(1.month-3.month)=0,324	P(Preop-3.month)<0,001 P(1.month-6.month)=0,004	P(Preop-6.month)<0,001 P(3.month-6.month)=0,864	
***P value for PRP	P(Preop-1.month)=0,272 P(1.month-3.month)=0,085	P(Preop-3.month)<0,001 P(1.month-6.month)<0,001	P(Preop-6.month)<0,001 P(3.month-6.month)=0,826	
***P value for Steroid	P(Preop-1.month)=0,002 P(1.month-3.month)=1	P(Preop-3.month)<0,001 P(1.month-6.month)=1	P(Preop-6.month)<0,001 P(3.month-6.month)=1	

Friedman Test - Kruskal Wallis Test Post Hoc Test: nonparametrikposthoc test (Miller(1966) *Median±IQR(Inter QuartileRange)

**P Value: Change VAS in group. *P value: Change VAS between groups

Table 3. Inter and intra group statistical evaluation of grip strengths.

	GROUPS					
	AB		PRP		Steroid	
	(Affected) /(Non-Effected)	*P value	(Affected) /(Non-Effected)	*P value	(Affected) /(Non-Effected)	*P value
GripstrengthPreoperative	(23,0±9,3) / (25,4±11,0)	0,496	(20,9±7,9) / (22,4±10,4)	0,617	(22,5±8,1) / (26,1±8,4)	0,207
Gripstrength 1. month	(25,0±9,4) / (26,2±10,8)	0,737	(22,7±9,8) / (23,4±10,0)	0,815	(24,4±10,0) / (26,4±8,8)	0,551
Gripstrength 3. month	(25,4±9,7) / (26,2±10,5)	0,814	(24,8±10,5) / (25,0±9,2)	0,947	(24,5±8,9) / (26,4±8,1)	0,524
Gripstrength 6. month	(25,1±8,7) / (27,1±10,7)	0,567	(26,4±10,7) / (25,3±9,1)	0,738	(24,1±9,2) / (26,4±8,1)	0,459
**P value (R) / (L)	0,097 / 0,362		0,071 / 0,127		0,281 / 0,467	

General Linear Model Repeated Anova (Wilks' Lambda - Huynh-Feldt) Independent T Test. **P value: Change Gripstrength in group.

*P value: affected/ non-affected Gripstrength

($p=0.003$). The comparison of the decrease in the six-month score in the AB group and that in the PRP group revealed no significant difference [$p(A-B)=0.301$]. But the comparison of the decrease in symptom scores in the AB and the PRP groups and that in the SE group showed a significant difference between the groups [$p(A-C)=0.017$, $p(B-C)=0.001$]. The decrease at the

six-month follow-up was 40.6 ± 22.2 in the AB group, 47.6 ± 16.5 in the PRP group and 23.8 ± 20.4 in the SE group (Table 1). The changes in Quick DASH scores after the application of PRP, AB and SE at months 1 and 6 are shown in Figure 1. The comparison of the decrease in preoperative VAS scores and the six-month VAS scores revealed a significant difference between

the AB, PRP and SE groups ($p=0.001$). The comparison of the decrease in VAS scores in the AB and SE groups and that in the PRP group at the six-month follow-up showed a significant difference [$p(A-B)=0.026$, $p(B-C)=0.001$]. The decrease in VAS scores between the AB and SE groups showed no significant difference at either the three- or six-month follow-ups ($p=0.342$) (Table 2). Figure 2 shows the changes in the VAS scores and their distribution between the groups. The grip strengths of the healthy upper extremity and the upper extremity with lateral epicondylitis were separately evaluated in the preoperative period and at the follow-ups.

There were no significant differences between grip strengths of both upper extremities (affected and non-affected arms were compared) between the groups and in each group individually ($p>0.05$) (Table 3).

Discussion

The mechanism of action of local steroids is uncertain. Corticosteroids, with their anti-inflammatory effect on tissue surfaces, have been reported to have the ability to suppress ectopic neural discharge when infiltrated into freshly cut nerve-endings. This ability has been attributed to the membrane-stabilizing effects of corticosteroids [6,7]. Several studies which have addressed the efficacy of SE demonstrated that steroids particularly reduced acute symptoms. On the other hand, it has also been reported that the incidence of recurrence is high in the long-term. In this study, patients were followed up for six months in an attempt to determine whether clinical improvement was prolonged in three groups of patients to whom local medication was administered.

In a study by Altay et al., the efficacies of 2 milliliters (ml) of lidocaine versus 1 ml of lidocaine combined with 1 ml of triamcinolone were compared, and no significant difference was noted between the two groups of patients who were followed up for one year. It was suggested that because the injection of local anesthetics had no long-term effect on the treatment of

lateral epicondylitis, the peppering technique might have played a role in the healing [8]. In our study, the procedure was performed by the same surgeon using the same technique in all of the patients to rule out the effects of the technique. In a study by Saartok et al., the effects of the administration of 6 milligrams (mg) of local betamethasone via injection and oral placebos to one group and the administration of 250 mg of naproxen combined with the local injection of saline (as a placebo) to the other group per day for two weeks were compared. At the two-week follow-up, five of the 10 patients in the naproxen group and five of the 11 patients in the injection group had improved, but there was no significant difference in effect between the two groups [9]. In a systematic review by Krogh et al., a total of 1,381 patients were evaluated, and the effectiveness of all injection therapies used for the treatment of lateral epicondylitis was compared. In this review, it was found that 10 out of 17 trials of injection therapies in the literature attempted to evaluate the effects of local injections of steroids and concluded that steroids were no more effective than placebos [10]. The results of the mentioned review also confirmed that AB, PRP, prolotherapy and hyaluronic acid were superior to placebos; however, no long-term outcomes were reported. As documented in these studies, the short-term efficacy of treatment protocols for lateral epicondylitis has directed most researchers to treatment protocols that are predicted to be successful in the long-term. In this study, patients with lateral epicondylitis who received local injections were followed up for six months. We believe, however, that longer-term assessments will allow for more effective evaluation of outcomes.

In a systematic review of 21 studies by Rabago et al., a significant improvement was observed in visual analog scale scores and in the grip strength of the patients receiving AB injections [11]. They suggested that autologous blood, together with the action of growth factors, suppressed inflammation that becomes chronic in the disease course. We believe that the improvement

observed in the short-term which does not last long with steroid treatment could be prolonged by the administration of AB together with the action of growth factors, the hypothesis on which our study was based. We found that there was a significant difference, particularly in Quick-DASH function scores, in patients receiving AB injections in the long follow-up period, but no significant difference was noted in short-term outcomes.

PRP treatment aims to improve the process of tissue repair through the delivery of bioactive agents which will provide chemotactic, proliferative and anabolic cellular responses. The purpose of concentrating blood is to obtain large amounts of bioactive growth factors in a low concentration. There is no consensus yet on the optimal concentration of platelets and growth factors in PRP for an effective treatment [12-14]. A study of 100 patients conducted in two teaching hospitals in the Netherlands by Joost C. Peerbooms et al. reported that the one-year outcomes of 51 patients receiving PRP were better than patients receiving SE, and that 37 (73 percent) of the 51 patients displayed significant improvement [15]. In this study, we found that the results of the patient group receiving PRP and followed up for six months were superior to those receiving steroid injections. Even though the superiority of PRP has been reported in a number of studies in the literature, there are few studies comparing AB to PRP. In our study, there was no statistically significant difference in functional scores between the efficacy of AB and that of PRP. Accordingly, to the best of our knowledge, this study is the first in the literature to demonstrate that the efficacy of PRP, with its associated high costs and difficulty of administration, was not superior to AB, which appears to have the ability to exert the same effects.

There are several limitations to this study. The number of patients was small because it was a single-center study, and future studies with longer follow-up periods are warranted. Those studies will evaluate function-

al outcomes and the efficacy of the treatment methods administered in the long-term, as well as observe whether full recovery can be achieved. In addition, we believe that the use of methods such as radiological imaging, which aim to increase the qualitative data of diagnostic and follow-up results in the pre- and post-operative periods, would yield more objective results. The strength of this study is that three methods with documented efficacy were randomized, and the effects of each treatment method on functional scores were followed up and assessed by a different researcher. In addition, the evaluation of muscle strengths of patients and the demonstration of whether changes in grip strength were correlated with functional scores indicate that this study is also qualitatively strong.

Conclusion

Considering the cost-effectiveness of the six-month follow-up period, PRP treatment should be resorted to as the last treatment choice in patients planning to undergo surgery. This study has proven that the administration of AB, rather than SE, would constitute a better treatment option in patients with long-term complaints who had previously received no injections. Recent advances in PRP kits and reductions in costs indicate that PRP will be the first-choice treatment option in the future.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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