Comparision of platelet-rich plasma and steroid injection in the treatment of chronic lateral epicondylitis

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Aim. **Platelet rich plasma (PRP) is a biological treatment which stimulates the recovery response by the expression of growth factors from activated thrombocytes. This study aimed to compare the effects of PRP and steroid injections in patients diagnosed with and being followed-up for chronic lateral epicondylitis.**

Methods. **This prospective study included 60 patients diagnosed with and being followed up for chronic lateral epicondylitis. In the PRP group (N.=30), blood taken from the patients was centrifuged to separate PRP, which was then activated by calcium chloride and a single dose injection was applied using the peppering technique. In the steroid group (N.=30) a single dose methylprednisolone with local anesthetic injection was applied using the peppering technique. Clinical evaluation was made by the Mayo elbow score and a visual analogue scale (VAS).**

Results. **No major complications were seen in any patient. Both groups Mayo elbow score was increased and VAS score was decreased and no statistically significant difference was detected between the groups at six weeks. Statistically significant better results in the Mayo elbow score and VAS score was determined in PRP group than steroid group at six months.**

Conclusion. **In the treatment of chronic lateral epicondylitis, although in the early stages the application of PRP showed similar effects to steroid injection, in the longer term PRP was more effective than steroid injection. PRP reduced pain and increased function in the treatment of chronic lateral epicondylitis. The application of PRP is a safe and effective method. Further studies are required to support the findings of this study.**

KEY WORDS: Platelet-rich plasma - Steroids - Tennis elbow - Endothelial growth factors.

Lateral epicondylitis is a painful condition which affects the tendinous tissue in the lateral epicondyle of the humerus and leads to loss of function in the affected extremity. The prevalence in the general population has been reported as 1-2%.[1] It is seen at equal rate in both genders and people aged 35-54 years are often affected.[2] Risk factors have been reported as repeated arm movements, movements requiring strength, cigarette smoking and obesity.[1]

Mechanical loading and inadequate microvascular response play a role in the pathomechanism of lateral epicondyli-

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tis.[3, 4] Hypovascular regions in the lateral epicondyle and elbow region have been reported in the depth of the common extensor tendons 2-3 cm distal to the lateral epicondyle.[5] Repeated microtrauma to the hypovascular base prevents healing and leads to lateral epicondylitis. The pathological tissue resembles granulation tissue formed from microscopic tears originating in the extensor carpi radialis brevis muscle. To repair this damaged tisssue, the body increases fibroblast proliferation together with local angiogenesis.[6] Nirschl and Pettrone [7] defined this tissue as angiofibroblastic hyperplasia.

Conservative treatment of lateral epicondylitis has been reported to reduce complaints in 90% of patients.[8] According to the concensus, treatment should firstly be conservative.[9] However, with conservative treatment the healing period can take up to 6-12 months and this process may be problematic both for the patient and the physician.[6] Conservative treatment choices include physical therapy, activity modification, splints, non-steroid anti-inflammatory drugs (NSAID), steroid injections, Extracorporeal shock wave therapy (ESWT) and benign neglect. No treatment method has been proven to be superior to any of the others.[10]

Platelet rich plasma (PRP) is a treatment form stimulating natural healing steps through growth factors contained in the platelets. PRP applied to the wound area accelerates the physiological healing process, provides support for the connection of cells, reduces pain and has an anti-inflammatory and anti-bacterial effect.[11] Obtaining PRP growth factor is a simple, cheap and easy way.[12] As it is autogenous in origin, easy to prepare and has an excellent reliability profile, it has opened the door to new treatment.[13]

Studies in literature have reported the use of PRP in lateral epicondylitis and chronic tendinopathy.[14-21] There are 16 concentration systems which can be used to obtain PRP. Leukocytes and growth factor contained in PRP are obtained in different amounts from these systems.[22] Apart from the concentration systems, PRP can be obtained manually from peripheral blood.[23, 24] Unanswered questions remain related to the application of PRP, such as the ideal volume, application frequency, application period and platelet activation.[25]

The aim of this study was to determine the effects on pain and function of PRP obtained manually as a cheap and easy method in the treatment of lateral epicondylitis and to compare these data with that of steroid injection which is often used in clinical practice. The hypothesis was that a single dose of manually-prepared PRP would reduce pain associated with lateral epicondylitis and increase function and that this effect would be superior to the frequently-used steroid injection.

Materials and methods

This was a prospective, comparative, clinical study. Approval was granted by the Local Ethics Committee and informed consent was obtained from all patients participating in the study. Patients who had been diagnosed with lateral epicondylitis and had been monitored for at least three months and shown no benefit from conservative treatment were included in the study. Exclusion criteria were systemic disease, pregnancy, active tumor or hematological malignant disease, infection, a history of anticoagulant use, Hb value <11 g/dL, thrombocyte count <150,000 mm^3, previous steroid injection to the elbow area or ESWT therapy, a history of elbow fracture or surgery in the elbow area.

A total of 60 patients who met the defined criteria were included in the study. The patients were separated into two groups of 30 each; the PRP group and the steroid group. Patients informed about the treatment options either with PRP or steroid. Patients who were accepted PRP treatment separated into PRP group; others were separated into steroid group. A single dose of PRP was administered to the PRP group. A mixture of 1 mL/40 mg methylprednisolone and 1 mL prilocaine was applied to the steroid group. The peppering injection technique

was used, injecting four to five different locations of fascia for both groups.

The preparation and application of PRP was made by the same researcher (F.S.) to all the patients in that group under the same conditions. The method described by Anitua [23, 24] was used. A total of 30 cc peripheral blood was taken from antecubital region of the patients into tubes containing 3.2% sodium citrate. The tubes were centrifuged at 1800 rpm for eight minutes at room temperature. From the 3.5 ml PRP which was obtained, 1 mL was sent to the laboratory for bacteriological test and platelet count. After activation, the 2.5 mL PRP containing 5.5% calcium chloride (Cl_2Ca) (50 µL Cl_2Ca in 1 mL PRP) was administered to the lateral epicondyle's maximal tenderness area with palpation under sterile conditions (Figure 1). The patient remained in a supine position for 20 minutes following the administration. The result of the laboratory evaluation of the obtained PRP determined that the platelet count per mL increased by 400% compared to the thrombocyte count.

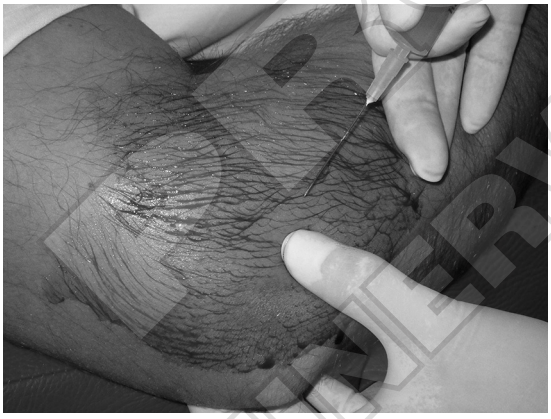

Figure 1.—PRP injection to elbow with peppering technique.

In the follow-up of both groups, standard stretching and strengthening exercises were given to the patients. No NSAID or splint was given to any patient. For the PRP group patients, rest was recommended for the first day after the injection. Ice and paracetamol were recommended for the pain and swelling. Permission was given for the use of anti-inflammatory medication for seven days after PRP administration.

The patients were evaluated clinically pretreatment and at the sixth week and sixth month of follow-up. In the clinical evaluation, Mayo elbow score and the Visual Analogue Pain Scale (VAS) were used. The patients were questioned with regard to side effects and subjective satisfaction.

Statistical analysis

Results were stated as mean±standard deviation (SD). Data were evaluated using SPSS software program (Windows Version 16.0). In the statistical evaluation of mean values between groups, Chi-square test, Student's *t*-test and MannWhitney U-test were used. The changes over time of the mean clinical scores of the groups were evaluated using Mann Whitney U-test. A value of $P<0.05$ was accepted as statistically significant.

Results

The patients of both groups were similar in terms of age, gender, side, and initial Mayo elbow and VAS scores (Table I). No

TABLE I.—*Comparison of patients characteristics at baseline.*

	PRP Group N.=30	Steroid Group N.=30	P value
Age (year)	49.8±8.4	51.1±7.4	0.519*
Male/Female	4/26	4/26	1
Affected elbow			
Right/Left	16/14	15/15	0.796**
Mayo elbow score	54.8±8.6	53.3±7	0.464***
VAS	8±1	8.1±0.9	0.876***

*T test; **Chi-Square test; ***Mann-Whitney test.

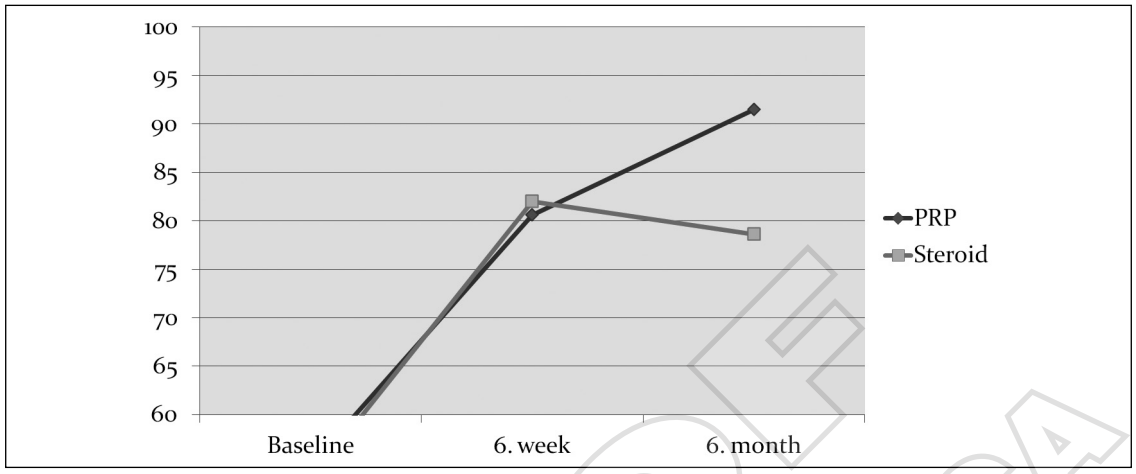

Figure 2.—Mayo elbow scores of both groups at baseline, week six and month six.

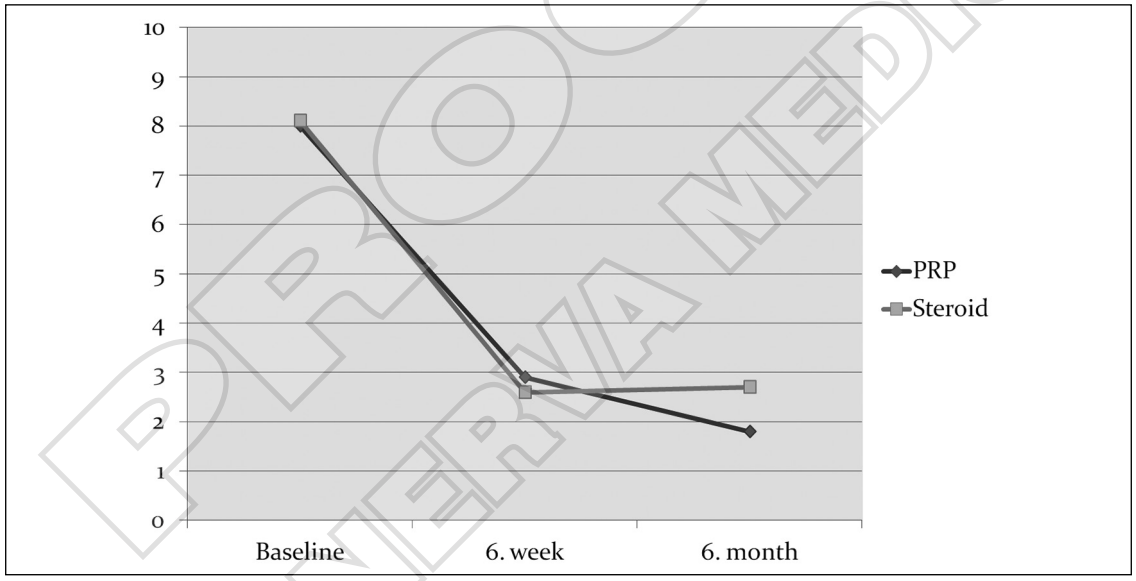

Figure 3.—VAS scores of both groups at baseline, week six and month six.

statistically significant difference was determined between the groups in terms of these factors.

In the PRP group, pain and mild swelling was determined in twelve patients after the injection. All complaints were resolved with the application of ice and paracetamol. Except this local complication in the PRP group, no complications were seen in any patient during the application or follow-up.

In the PRP group, the mean Mayo elbow score was 80.7±8.5 at the sixth week follow-up and 91.5±5.9 at the six month follow-up (Figure 2). The mean VAS score was determined as 2.9±1 at sixth week and 1.8±0.8 at six months (Figure 3). Compared to the pre-treatment scores, the difference between the sixth week and six month scores was statistically significant.

In the steroid group, the mean Mayo elbow score was 83.3±9.8 at the sixth week follow-up and 78.7±7.3 at the six month follow-up (Figure 2). The mean VAS score was determined as 2.6±1 at sixth week and

TABLE II.—*Comparison of Mayo elbow and VAS scores of groups at baseline, week six and month six.*

	PRP Group N.=30	Steroid Group N.=30	P value*
Mayo elbow score			
Baseline	54.8±8.6	53.3±7	0.464
6. week	80.7±8.5	83.3±9.8	0.230
6. month	91.5±5.9	78.7±7.3	<0.001
VAS			
Baseline	8±1	8.1±0.9	0.876
6. week	2.9±1	2.6±1	0.211
6. month	1.8±0.8	2.7±1.1	<0.001

*Mann-Whitney test.

2.7±1.1 at six months (Figure 3). Compared to the pre-treatment scores, the difference between the sixth week and six month scores was statistically significant.

When the mean Mayo elbow and VAS scores at the sixth week and six month follow-up of the groups were compared with each other, there was no statistically significant difference between the groups at the sixth week. But the clinical scores of the PRP group were determined to be statistically significantly higher at the sixth month (Table II).

Discussion

The term lateral epicondylitis expresses an inflammatory condition. However, Nirschl examined the histology of pathological tissue and findings of inflammation were not determined. The term, angio-fibroblastic tendinosis was recommended.[26] Even when there are no inflammatory cells in lateral epicondylitis, patients experience severe pain with activity. It has been reported that increased glutamate and substance-P Calcitonin gene-related peptides in the nerve tissue which originates in the extensor carpi radialis brevis leads to pain *via* the neurogenic route.[27, 28]

Steroid injection is often used in the conservative treatment of lateral epicondylitis and is effective in the short-term.[29] However, skin de-pigmentation, fat atrophy, cases of tendon ruptures,[30] and osteomyelitis [31] have been reported associated with steroid injections. In the current study, the functional scores of the steroid group patients at the sixth week were determined to have increased compared to the baseline values and the pain scores had decreased. However, the effect provided in the short-term did not continue at the sixth month follow-up as the functional scores were determined to have decreased and the pain scores to have increased. In conformity with literature, the steroid injection treatment in the current study was effective in the short-term. No complications were observed in any patient of the steroid group.

PRP was first used in 1987 in heart surgery to prevent excessive blood transfusion.[32] Several studies have reported the use of PRP in lateral epicondylitis and chronic tendinopathy.[14-21] More than 30 bioactive proteins are found within the alpha granules of platelets.[24] Growth factors such as platelet-derived growth factor, transforming growth factor, vascular endothelial growth factor and insulin like growth factor and proteins such as fibrin, fibronectin, vitronectin, and thrombospondin, which are found in PRP, play a role in many stages of tissue healing. The growth factors activate some of the cells which have a function in tissue healing and thus provide soft tissue healing and bone regeneration.[12]

PRP stimulates the proliferation of various cell types in cells and tissue,[33] and activates repair cells in the blood circulation.[34] With the effect of growth factors that it contains, it stimulates local stem cells and activates the repair cells in the circulation and the bone marrow. Excessive inflammation inhibits apoptosis and metalloproteinase activity.[35] Moreover, in tendon recovery, PRP increases tenocyte proliferation in the

injured area by providing revascularisation by means of the included growth factors, and is effective in increasing collagen expression in the tenocytes.[36]

Three different methods can be used to obtain PRP; automatic machines and commercial kits with double spin rotation, single spin rotation and manual PRP separation and selective blood filtration (plateletpheresis). Anitua [23] reported that a platelet count over 300,000/μL in PRP is effective. In another *in-vitro* study, platelet concentration 2.5 times greater than the basal platelet count was reported to be the most effective.[37] The prepared PRP is activated by adding bovine or human thrombin or calcium chloride.[38] Growth factors and cytokines are revealed with the formation of platelet gel from the activated PRP. In the current study PRP was prepared as single spin rotation and manually. In the analysis of the prepared PRP, concentration was determined as four times greater than the thrombocyte count in the peripheral blood. The prepared PRP was activated by the additon of calcium chloride.

In the evaluation of the findings of the current study, at both six weeks and six months after application, the functional scores of the PRP group were determined to have statistically significantly increased compared to the baseline values and the pain scores were determined to have statistically significantly decreased compared to the baseline values. When the groups were compared with each other, although there was no statistically significant difference between the groups at the sixth week, the clinical scores of the PRP group were determined to be statistically significantly higher at the sixth month. In a study by Mishra *et al.*[14] PRP was applied to 15 patients diagnosed with chronic lateral epicondylitis and bupivacaine was administered to a control group of 5 patients. At a mean 25.6-month follow-up, evaluation by Mayo elbow score and VAS determined a 93% pain reduction in the PRP group patients compared to the initial values. Peerbooms *et al.*[15] applied steroid injection to 49 patients and PRP to 51 patients. The patients were evaluated with disabilities of the arm, shoulder and hand (DASH) and VAS and at the end of the first year the DASH score (73%) of the PRP group was reported to be better than that of the steroid group (51%). At the two-year follow-up of the same patients, Gosens *et al.*[16] reported that the DASH scores of the steroid group, which had decreased from the initial level, were better than the scores of the PRP group. Under ultrasound guidance, Thanasas *et al.*[17] applied 3 mL PRP to 14 patients and 3 mL of autologous blood injection (ABI) to 14 patients. The patients were followed-up for six months using the Liverpool elbow score and VAS. While no difference was found between the groups in the elbow score, the VAS score of the PRP group was reported to be lower. Creaney *et al.*[18] compared PRP and ABI and found no differences in Patient-Related Tennis Elbow Evaluation (PRTEE) in a six-month follow-up. However, they reported higher rate of conversion to surgery in ABI group. In a randomised, placebo-controlled, double-blind study by Krogh *et al.*[19] PRP was applied to 20 patients, steroid to 20 patients and saline to 20 patients. No difference was determined between the groups in the third month using the PRTEE and evaluations of tendon thickness by USG and Doppler. Chaudhury *et al.*[20] reported sonographic assessment of extensor tendon morphology and vascularity following injection of PRP in six patients. They reported a trend for increased vascularity at the myotendinous junction up to six months. In the current study, although a clinical recovery was determined over a six month follow-up, it is not yet known how long this effect will last.

The manual method of obtaining PRP used in the current study is low-cost and effective. While the cost of automatic devices and kits to obtain PRP is several hundreds of dollars, the cost of the manual method used to prepare PRP was approximately ten dollars.[39]

For PRP obtained from autologous blood, there is no risk of immune reaction or disease transfer. There are no studies in literature warning of hyperplasia, carcinogenisis or tumour growth of PRP.[11] No major com-

plications were encountered in any patient in the PRP group of the current study. Pain and mild swelling in twelve patients was determined to have been resolved within a few days with ice and paracetamol.

The limitations of this study are that it was not randomised, there was no placebo control group, there were no radiological and biological results during follow-up to be compared with the functional and pain scores, the number of patients was low and the follow-up period was short.

Conclusions

The results of this study have shown that the administration of PRP in chronic lateral epicondylitis treatment, although in the early stages showed similar effects to steroid injection, in the longer term PRP was more effective than steroid injection. PRP reduced pain and increased function in the treatment of chronic lateral epicondylitis. The application of PRP is a safe and effective method. However, prospective, randomised, placebo-controlled, multi-centre studies are required to clarify these results and better understand the effects of PRP.

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