



A randomized study of autologous conditioned plasma and steroid injections in the treatment of lateral epicondylitis

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Abstract

Purpose Chronic tendinopathy of lateral epicondyle of the humerus, commonly known as “tennis elbow” is one of the most frequent tendinopathies caused by recurrent overload of the muscle origins. The aim of the study was to assess the effectiveness of treating lateral epicondylitis (LE) with autologous conditioned plasma (ACP) and betamethasone injections, and to compare these methods over the course of a one year follow-up.

Methods Patients were randomly placed into one of two groups: 53 were treated with ACP, and 46 with 1 ml betamethasone injections and 2 ml of 1 % lignocaine. Both those groups were comparable in terms of initial DASH score. **Results** After six weeks and six months, the mean DASH score was significantly better in the betamethasone group, but was better in ACP group after one year. Full recovery (patients with no symptoms) at all time points was more common in the betamethasone group. A comparison of grouped DASH scores revealed more *very good* and *good* results in the ACP group after one year. More patients had pain symptoms related to injection in the ACP group than the betamethasone group.

Conclusions ACP therapy of LE allows better results to be obtained at 12 months. Betamethasone injections give more

rapid improvement, but the therapeutic effect is longer lasting in the ACP group.

Keywords Tennis elbow · Conservative treatment · PRP · ACP · Steroids

Introduction

Chronic tendinopathy of the lateral epicondyle of the humerus, commonly called *tennis elbow*, is one of the most frequent tendinopathies caused by recurrent overload of the muscle origins [1].

The literature proposes several options for treating lateral epicondylitis (LE), including activity modification, physical therapy, operative treatment, pharmacotherapy, of the injection of botulinum toxin, steroids, platelet rich plasma (PRP), autologous conditioned plasma (ACP) [2–13]. The origins of ACP and PRP usage were connected with dentistry and plastic surgery, and then later in Orthopedics and especially in sports medicine [14, 15]. ACP is a concentrated extract of platelets from autologous blood with their secreted growth factors which are one of the factors responsible for healing. The use of this preparation is particularly important as a treatment option in soft tissue disorders where the healing response has failed and the resulting inflammation has caused a chronic condition. An autologous preparation injected into the area of the tendinopathy initiates a healing response [16, 17].

Previous studies have compared steroid injections with PRP, but not with ACP. The aim of the study was to assess the effectiveness of the treatment of LE with autologous conditioned plasma (ACP) and betamethasone injections and to compare these methods over the period of a one year follow-up.

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Materials and methods

This prospective, randomized study was performed between the years 2009 and 2011. Patients with lateral epicondylitis were randomly placed into one of two groups: the first group was treated with ACP (Double Syringe System, Arthrex) and the second with a combination of 1 ml betamethasone injections and 2 ml of 1 % lignocaine. A computerised randomisation schedule was prepared by an independent researcher (MS), and using concealed allocation each patient was assigned to one of the two treatment methods using the computer generated sequence. The inclusion criteria were as follows: clinical diagnosis of lateral epicondylitis for more than six weeks, lack of conservative treatment of lateral epicondylitis for at least six weeks before betamethasone/ACP therapy and informed consent obtained from the patient. Patients who failed to attend one of the follow-up visits, refused to participate in study or had previous operative procedures of the elbow were excluded.

Sixty-four patients who met the inclusion criteria were included in the first group and 56 in the second. Fifty-three patients (28 men and 25 women) from the ACP group and 46 (12 men and 34 women) patients from the betamethasone group were available for final analysis. The mean age in the ACP group was 47.0 (range from 25 to 67 years), and 54.0 in the betamethasone group (range from 21 to 96 years).

The diagnosis of LE was performed on the basis of symptoms reported by patients and clinical examination: tenderness over extensor carpi radialis brevis origin as well as Cozen's test [18]. No ultrasound or radiographic examination was performed. The steroid injections were performed with the use of a 0.8 mm syringe. One ml of Diprophos (Schering-Plough Labo N.V., Belgium) (6.43 mg of Betamethasoni dipropionas and 2.63 mg of Betamethasoni natrii phosphas) and 2 ml of 1 % lignocaine were injected subcutaneously. The ACP injections were performed in the same way and prepared according to the manufacturer's instructions. Both Diprophos and ACP injections were done by the same physician (RL) in the same way in every case.

The DASH (Disabilities of the Arm, Shoulder and Hand) score was used for clinical assessment [19]. The score was collected at four points: just before betamethasone/ACP injection, at six weeks, and at six and 12 months. An increase of 15 points was considered as indicating an improvement, as recommended by the authors of the DASH score. For statistical analysis, a DASH score of 0–25 points was considered as very good, 26–50 as good, 51–75 as fair and 76–100 as poor. Two days after the injection, patients were asked whether or not they felt any pain.

The study was approved by the ethics committee of our institution.

Statistical analysis

The independent Chi square test was used to compare the frequency of occurrence of all parameters in the tested groups (comparison of full recovery, injection-related pain, grouped DASH score) at all time points. In the case of small counts in some fields of the table, the Yates correction was used. Before making comparisons of means, the normality of the distributions of the measurable traits were examined by the λ -Kolmogorov compliance test.

Because the distributions of the characteristics analysed in the study in each group were markedly not normal, non-parametric tests were used to compare means: the Mann–Whitney test was used to compare two independent groups and the Friedman test was used to compare a number of dependent groups. Friedman test was used to evaluate differences in the results of the DASH survey with time. As statistically significant changes were identified in the tests using point scores, the Wilcoxon pair test was then used as a post-hoc test.

To test dependence between parameters, the r linear correlation coefficient was used. In each tested group, at each stage of the study, a test was made of the dependence between age and the achieved point score. The significance of the correlation coefficient was evaluated using the Student's t -test. To assess the effect of age on the point score, a coefficient of determination was designated, which was the square of the correlation coefficient.

A p -value of less than 0.05 was considered to be statistically significant.

Results

Both those groups were comparable in terms of initial DASH score. At 6 weeks and 6 months, the mean DASH score was significantly better in the Betamethasone group, but at one year it was better in the ACP group. It can be seen that while the therapeutic effect occurs more quickly in the Betamethasone group, it lasts longer in the ACP group (Table 1). An analysis of DASH score within groups at different time points showed gradual improvement over initial status in both the ACP and betamethasone groups ($p < 0.001$ and $p < 0.001$, respectively).

Table 2 presents the results illustrating the degree of full recovery, i.e., the number of patients who reported no symptoms, at different time points. Those results favor the betamethasone group (Table 2). A comparison of grouped DASH scores at different time points reveals no statistically significant difference between the first three time points: before treatment, at six weeks and six months. At one year, more very good and good results were noted in the ACP group and fair results in the betamethasone group (Table 1). Two days after injection, more patients reported pain symptoms related to

Table 1 Comparison of DASH score in ACP and betamethasone group at different time points

	ACP group; <i>n</i> =53			Betamethasone group; <i>n</i> =46			Z value	P value
	Range	Mean	Median	Range	Mean	Median		
Before treatment	22.5–94.2	53.2±15.5	49.2	27.8–88.7	58.6±14.8	53.3	1.849	<i>p</i> >0.05
At 6 weeks	2.5–66.7	32.2±18.2	33.2	0–68.2	20.6±21.5	10.0	3.041	<i>p</i><0.01
At 6 months	0–42.5	14.2±13.4	10.0	0–68.8	14.7±22.0	14.7	2.185	<i>p</i><0.05
After 1 year	0–66.7	9.9±17.1	2.5	73.0	14.4±25.2	13.0	1.445	<i>p</i><0.05

P-values marked in bold are statistically significant

ACP autologous conditioned plasma, SD standard deviation

injection in the ACP group than in the Betamethasone group: 44 (96 %) patients from betamethasone group and 42 (79 %) from ACP group were free of pain (*p*<0.05).

No statistically significant difference was observed between age and DASH score at any time point in either group (*p*>0.05 for all).

Discussion

A number of studies make direct comparisons between the results of using a platelet-rich plasma preparation and steroid preparations to treat tendinopathy of the lateral epicondyle of the humerus [6–8, 10, 19]. However, a literature review reveals no work comparing the results of therapy using ACP preparations and those based on steroid preparations. Generally, literature focused on ACP application for LE is rather scarce [20, 21]. Our present findings demonstrate the efficiency of ACP therapy compared to betamethazone. In the group of patients treated with ACP, the number of results below 25 points at the end of the observation period equalled 43 (81 %), with 2 (4 %) results higher than 50 points. The therapeutic effect was found to be slower than that of betamethazone: the number of scores higher than 50 points at the start of treatment was 24, 11 after six weeks, zero after six months, and at the end of the observation period, the number insignificantly rose to 2 Table 3.

In the group of patients treated with betamethazone, 36 (78 %) very good results were noted by the end of the observation period. As the period of observation progressed, the number of scores over 50 points increased, with a fairly sharp fall at the beginning

of therapy. On the day the preparation was given, the number of scores above 50 points was 30, which sharply fell to six at six weeks of treatment, with only three such scores being recorded at six months. However, nine were noted at 12 months (20 %).

These results correspond to data published by Peerbooms et al. - a work comparing the results of treating patients with tendinopathy of the lateral epicondyle of the humerus with the use of PRP and steroid injections [6]. Considering that a reduction in the DASH point scores by at least 25 % was considered a success over the one year observation period, as many as 73 % of the treatments with PRP were successful compared to 49 % treated by steroid injections. In addition, a quicker therapeutic effect was noted for steroid injections compared to platelet-rich plasma, although the effect was not as long lasting. These same group evaluated the same group of patients for two years from the administration of injections, achieving better results in the group treated with platelet-rich plasma preparations when returning to baseline than patients treated with steroids [7]. A similar conclusion regarding the short-term beneficial effects of steroid therapy may be found in Coombes et al. [8].

The most recent report comparing platelet-rich plasma, steroid and saline solution therapies is that of Krogh et al. [10]. The authors compare three groups of 20 patients, treated with the three preparations for a period of three months. The patients were evaluated on the basis of a PRTEE questionnaire and USG scan. The authors did not find any advantage to therapy using platelet-rich plasma or steroids over the control group administered with physiological saline during the final observation period. However, they discuss the fast reduction of painful symptoms in the group treated with steroids. The same

Table 2 Comparison of full recovery in ACP and betamethasone group in different time points

	ACP group; <i>n</i> =53		Betamethasone group; <i>n</i> =46		Chi ² value	P value
	N _e	%	N _e	%		
At 6 weeks	0	0 %	8	17 %	8.823	<i>p</i><0.01
At 6 months	8	15 %	28	61 %	22.299	<i>p</i><0.001
After 1 year	19	36 %	30	65 %	8.497	<i>p</i><0.01

P-values marked in bold are statistically significant

Table 3 Grouped DASH scores at different time points

DASH (points)	Before treatment		At 6 weeks		At 6 months		After 1 year	
	ACP group N _e	B group N _e	ACP group N _e	B group N _e	ACP group N _e	B group N _e	ACP group N _e	B group N _e
0–25	2(4 %)	0 (0 %)	32 (43 %)	27 (59 %)	38 (72 %)	32 (70 %)	43 (81 %)	36 (78 %)
26–50	27 (51 %)	16 (35 %)	19 (39 %)	13 (28 %)	15(28 %)	11(24 %)	8 (15 %)	1 (2 %)
51–75	18 (34 %)	23 (50 %)	11 (21 %)	5 (13 %)	0 (0 %)	3 (6 %)	2 (4 %)	9 (20 %)
>76	6 (11 %)	7 (15 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
<i>P</i> value	<i>p</i> >0.05		<i>p</i> >0.05		<i>p</i> >0.05		<i>p</i><0.05	

P-values marked in bold are statistically significant

B group Betamethasone group

group also demonstrate a reduction in the thickness of the tendon as well as the doppler activity of the USG evaluation.

Thanasas et al. compare treatment using platelet-rich plasma and normal blood from a patient [9]. They examined two groups of 14 patients after six weeks, three months and six months after administration of preparations on the basis of the VAS scale and the Liverpool Elbow Score. They report that 61.47 % of patients treated with platelet-rich plasma showed an improvement on the VAS scale compared to 41.6 % of the group treated with blood. No statistically significant difference in Liverpool Elbow Score was observed, and on the basis of the obtained results they conclude that platelet-rich plasma is as effective as a form of analgesic therapy. Similar findings were reported by Stenhouse et al., who compared ACP injections and ultrasound-guided dry needling. No significant difference between the two treatment groups was demonstrated at each follow-up interval [20]. Tetschke et al. demonstrated beneficial effects of autologous proliferative therapies (ACP) and low-level laser application in the treatment of lateral epicondylitis at one year follow up. Both groups showed a significant improvement in time response. [21].

Krogh et al. summarize the results of a meta-analysis including 17 controlled randomised studies regarding the treatment of tendinopathy of the lateral epicondyle of the humerus using a range of injections [10]. This group of studies included ten covering the application of steroids, four of botulin, three of autologous blood from the patient, two of platelet-rich plasma and one each for polidocanol, glucosaminoglycan, prolotherapy and hyaluronic acid. The greatest difference in results with regard to placebo was noted during treatment with hyaluronic acid and prolotherapy while the next place was occupied by autologous blood from the patient and platelet-rich plasma, which both brought significantly better results. A marginal improvement was found during botulin therapy, with steroids, glucosaminoglycans and polidocanol giving no clear advantage over placebo.

The use of ACP has only been addressed by Deans et al. and concerned therapy of chronic tendinopathy of the Achilles

tendon [22]. The author tested 26 patients with tendinopathy of the Achilles tendon which had lasted for at least six months. A significant improvement was obtained in the reduction of pain symptoms, as well as improved quality of life and ability to take part in sporting and everyday activities. ACP was also used in treating tendinopathy of tendons in horses. Georg et al. administered the preparation to damaged tendons in seven horses followed by repeated injections after two weeks.

The study has some limitations. Despite the fact that patients were randomized on two groups, the study was not blinded to the researchers and participants, so both groups were aware what kind of treatment was applied. Furthermore, patients were not selected do the study on the basis of gender, occupation or kind of sport activity, what may potentially influence the outcome.

It may be concluded that ACP therapy of LE allows better results to be obtained at 12 months. Betamethasone injections give more rapid improvement, but the therapeutic effect is not as permanent as in the ACP group.

Conflict of interest The authors declare that they have no conflict of interest.

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