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SHOULDER

The effect of subacromial injections of autologous conditioned plasma versus cortisone for the treatment of symptomatic partial rotator cuff tears

Lutz von Wehren[1] · Fabian Blanke[2] · Atanas Todorov[1] · Patricia Heisterbach[1] · Jannis Sailer[1] · Martin Majewski[1]

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Abstract
Purpose Rotator cuff tears are one of the most common causes of shoulder malfunction and pain, which lead to a significant reduction in the quality of life. This present study investigated the effects of subacromial platelet-rich plasma injections [i.e. autologous conditioned plasma (ACP) injections] as compared to standard subacromial cortisone injection therapy in 50 patients with partial rotator cuff tears.
Methods Before injection, and 6 weeks, 12 weeks and 6 months thereafter, the patients were assessed by the Constant–Murley score (CMS), the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES), the simple shoulder test (SST) and a pain visual analogue scale (VAS). An MRI was also performed before and 6 months after injection.
Results Both patient groups had statistically significant better shoulder score outcomes over time. ASES, SST and CMS outcomes after 12 versus 6 weeks were better in the ACP group as compared to the cortisone group. VAS, ASES and CMS outcomes after 12 weeks versus baseline in the ACP group were better as compared to the cortisone group. There was a statistically significant difference between ACP group and cortisone group 12 weeks after injection regarding VAS, ASES, SST and CMS in favour of the ACP group. The MRI showed an improvement in grade of tendinopathy in both groups, however, without statistically significant differences between the two groups.
Conclusion Compared with cortisone injections, ACP injections show earlier benefit as compared to cortisone injections although a statistically significant difference after 6 months could not be found. Therefore, subacromial ACP injections are a good alternative to subacromial cortisone injections, especially in patients with contraindication to cortisone.
Level of evidence Therapeutic study, Level III.

Keywords Rotator cuff · Platelet-rich plasma · Autologous conditioned plasma · Subacromial impingement syndrome · Shoulder pain

Introduction

Due to its enormous range of motion, the shoulder is one of the most complex joints in the human body. Pathology of the soft tissues of the shoulder including the musculotendinous rotator cuff and subacromial bursa is extremely common and is a principal cause of pain and suffering [26]. Due to the relative avascular nature of tendons, the regenerative potential is limited [20]. Hence, orthobiologics such as platelet-rich plasma (PRP), platelet-poor plasma and autologous processed serum could be an option for the treatment of this pathology. They have first been used to facilitate tissue repair 25 years ago and have the ability to regenerate tissue [14]. Today, orthobiologics are commonly used in many orthopaedic applications, especially in the treatment of tendinopathies [14].

Platelet products represent an enriched autologous source of platelets, which contain granules filled with growth factors, delivering high concentrations of growth

✉ Martin Majewski
martin.majewski@usb.ch

[1] Orthopädie, Universitätsspital Basel, Spitalstrasse 21, 4031 Basel, Switzerland

[2] Klinik für Sportorthopädie und arthroskopische Chirurgie, Orthopädische Fachkliniken der Hessingstiftung, Hessingstrasse 17, 86199 Augsburg, Germany

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factors above physiological levels [41]. There is some clinical evidence that application of autologous platelets may help to revascularize the area of injury, to promote tendon healing and to improve pain and functional outcomes in rotator cuff pathologies [13, 32, 34].

To our knowledge, the effect of PRP injections on shoulders with partial rotator cuff tears as compared to standard injection therapy with cortisone has not been investigated yet. Therefore, this study evaluated PRP injections versus cortisone injections into the subacromial space in patients with painful partial tears of the supraspinatus tendon as confirmed by magnetic resonance imaging (MRI). The results should contribute to a better understanding of the role of PRP in treatment of symptomatic partial rotator cuff tears. This study hypothesized that subacromial injection of autologous conditioned plasma (ACP) in symptomatic partial rotator cuff tears had a better outcome than cortisone injection.

Materials and methods

Fifty consecutive patients (24 women and 26 men, mean age 54 ± 12 years) admitted to the University Hospital Basel unit Spital Oberengadin in Samedan between 2011 and 2014 were enrolled in this study. Before admission, all patients reduced their activities of daily living or suspended their sport activities due to their shoulder pain. Patients were included if they were ≥18 years, experienced persistent continuous pain in one shoulder for at least 2 months and had evidence of a partial supraspinatus tear. MRI was evaluated by two experienced radiologists.

Exclusion criteria were generalized inflammatory arthritis, including ankylosing spondylitis, rheumatoid arthritis or psoriatic arthritis, prior supraspinatus tendon tear, pregnancy, severe infection, known malignancy, bleeding disorder, nerve-related symptoms such as radiculopathy or osteoarthritis of the shoulder, previous extracorporeal shock wave therapy or corticosteroid injection into the shoulder.

All injections were performed by one of the authors. Point of injection was the lateral subacromial space below the lateral border of the acromion whilst directing the syringe to above the footprint of the supraspinatus tendon. After injection, all patients were allowed to move their shoulder but were advised to avoid sport activities for 4 weeks. NSAIDs were not allowed for 6 months. No physiotherapy was prescribed.

The first consecutive 25 patients received a cortisone injection [Dermapharm Kenacort® 40 mg (triamcinolone acetonide, crystal suspension)] by means of a 5-ml syringe under aseptic conditions.

The following 25 patients received ACP injections using Arthrex. This double-syringe system includes an outer 10-ml syringe and a smaller, inner syringe. Ten millilitres of autologous blood was taken from the antecubital vein with the outer syringe, placed into the Arthrex Centrifuge (Rotofix) and centrifuged for 5 min at 1500 rpm. During the extracorporeal blood processing, 2 ml of citrate dextrose was used to prevent clotting. The system allows supernatant the PRP transfer from the 10-ml outer syringe into the 5-ml syringe under aseptic conditions. Three sequential injections in 7-day intervals were performed in every patient.

Approval was obtained from the local medical ethics committee (Ethikkommission beider Basel, number 191/11) prior to the study.

Clinical evaluation

After 6 weeks, 12 weeks and 6 months, patients were examined in the outpatient clinic. Outcome measures were the Constant–Murley score (CMS) [9], the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES) [36] and the simple shoulder test (SST) [27]. All measures were reported to have a good reliability [31, 38]. Patients were also asked to rate their pain on a visual analogue scale (VAS) (zero indicating no pain and ten the worst possible pain). The subgroup force of the CMS was calculated for each age according to the table of Constant.

Radiological evaluation

MRI was performed using a 1.5-Tesla scanner (Siemens, Erlangen, Germany) before and 6 months after injection. Axial (T1, fat saturated), coronal (proton density, T1, T2, fat saturated) and sagittal (T1, fat saturated) views were obtained. All sequences were performed with a 16-cm field of view, 256 × 512 matrix and 3.5-mm slice thickness.

One of the two radiologists who evaluated the first MRI also was in charge to evaluate all shoulder MRIs performed at the follow-up examinations without specific assignment. The radiologists who did the MRI assessment did not know which kind of injection had been done. MRIs were scored on a 0–5 severity scale (modified from Lewis [26] by Scarpone et al. [42]): 0, no tendinopathy (normal tendon signal); 1, mild tendinopathy (tendon oedema); 2, moderate tendinopathy (tendon oedema, hypoechoic areas, neovascularization and/or bursal involvement); 3, moderate tendinopathy + partial thickness tear present; 4, severe tendinopathy (moderate tendinopathy + fatty infiltration) ± partial thickness tear present; and 5, severe tendinopathy + full thickness tear present.

Statistical analysis

A priori power analysis established a sample size of at least 17 in each group to detect a relevant difference of

at least 15 points (standard deviation 15 points) with the paired sample t test in the ASES and CMS scores with a power of 80 % ($b = 0.20$) on a 5 % significance level ($a = 0.05$). Paired sample two-tailed t test was used to analyse differences between pre- and post-infiltrative values (VAS, ASES, SST and CMS). Independent sample two-tailed t tests were used to analyse differences between ACP and cortisone group, also corrected for baseline, 6-week and 12-week data as appropriate. The Chi-square test was performed for gender, injection site and dropout comparisons. Fisher's exact test was performed for location of partial tendon rupture and MRI changes. Significance levels were set at 0.05. Statistical analysis was done using SPSS 19.0 software (SPSS Inc., Chicago, IL, USA).

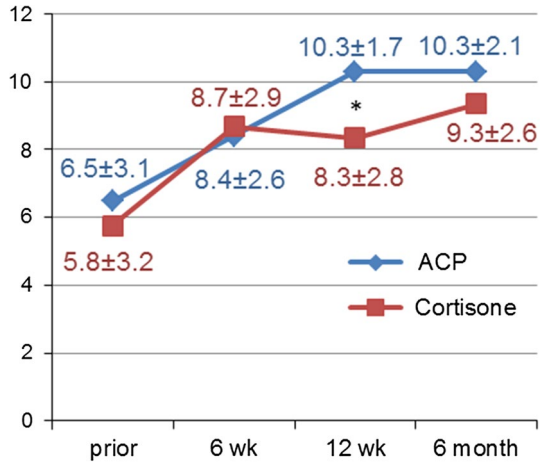

Fig. 1 SST of the ACP and cortisone groups over time (baseline, 6 weeks, 12 weeks and 6 months). *Asterisk* significant difference between the ACP and cortisone group

Results

Twenty-five patients (mean age 53 ± 14 years) participated in the ACP group and twenty-five patients (mean age 55 ± 10 years) in the cortisone group (n.s.). There were 12 men and 13 women in the ACP group and 14 men and 11 women in the cortisone group (n.s.). Fourteen injections into the right shoulder and 11 into the left shoulder were performed in the ACP group and 16 injections into the right shoulder and nine into the left shoulder in the cortisone group (n.s.). During the first 6 months, four patients dropped out in the ACP group and seven patients in the cortisone group due to shoulder surgery (n.s.). No infection was observed after injection in both groups.

Both patient groups had statistically significant better ASES, SST and CMS shoulder scores and pain relief in VAS after injection compared with the baseline before injection (Table 1).

Comparing both groups at all time points, patients in the ACP group were significantly better after 12 weeks in SST ($p = 0.02$) (Fig. 1), ASES ($p = 0.01$), CMS ($p < 0.01$) and VAS ($p = 0.01$) as compared to the cortisone group.

The difference in CMS in favour of the ACP group was particularly due to a better activities of daily living (ADL) ($p < 0.01$), range of movement (ROM) ($p = 0.01$) and force ($p = 0.04$) in the ACP group. After 6 months, ROM was significantly higher in the ACP group ($p = 0.03$).

There was a significant improvement in the ACP group as compared to the cortisone group 12 weeks versus baseline in ASES ($p = 0.02$) (Fig. 2), VAS ($p = 0.02$) and CMS ($p = 0.03$).

There also was a significant improvement in the ACP group as compared to the cortisone group 12 weeks versus 6 weeks in CMS ($p = 0.05$) (Fig. 3), SST ($p = 0.04$) and ASES ($p = 0.04$).

In the MRI data, statistical pre- and post-comparisons did not reveal any statistically significant differences between location of partial rupture (n.s.) and the grade of tendinopathy (n.s.) (Table 2).

Discussion

The most important findings of the present study were better shoulder scores after 12 weeks in the ACP group in comparison with the cortisone group. VAS and shoulder scores (ASES, SST and CMS) were statistically significant

Table 1 p values of paired t tests of the ACP and cortisone group for ASES, SST and CMS

Group	Score	Baseline—6 weeks	Baseline—12 weeks	Baseline—6 months	6–12 weeks	6 weeks–6 months	12 weeks–6 months
ACP	ASES	<0.01	<0.01	<0.01	n.s.	n.s.	n.s.
	SST	<0.01	<0.01	<0.01	n.s.	0.03	n.s.
	CMS	<0.01	<0.01	<0.01	n.s.	0.04	n.s.
Cortisone	ASES	<0.01	<0.01	<0.01	n.s.	n.s.	n.s.
	SST	<0.01	<0.01	<0.01	n.s.	n.s.	n.s.
	CMS	<0.01	<0.01	<0.01	n.s.	n.s.	n.s.

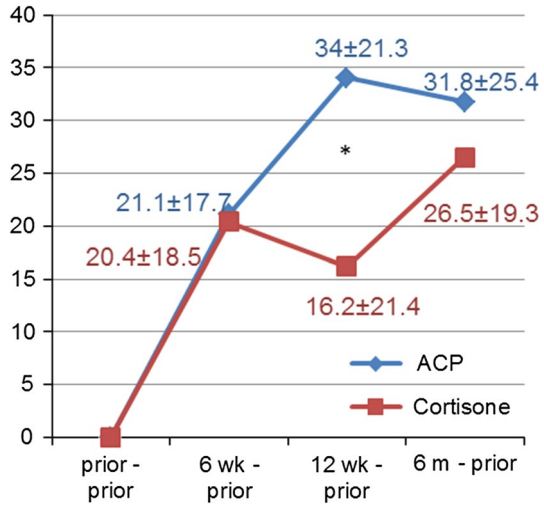

Fig. 2 Improvement in ASES compared with baseline of the ACP (50.7 ± 15) and cortisone group (50.6 ± 14) over time (6 weeks, 12 weeks and 6 months). *Asterisk* significant difference between the ACP and cortisone group

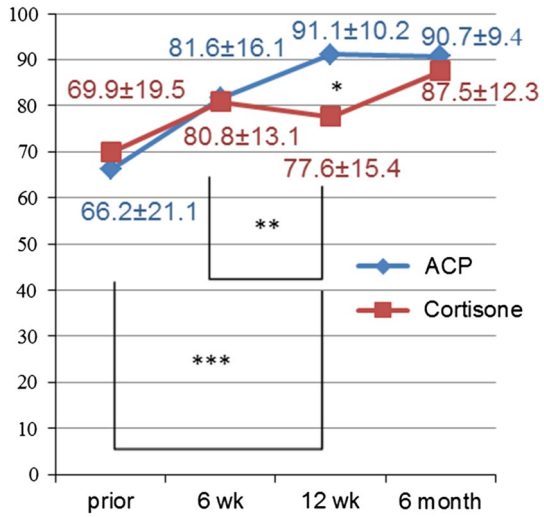

Fig. 3 CMS of the ACP and cortisone groups over time (baseline, 6 weeks, 12 weeks and 6 months). Single *asterisk* significant difference between the ACP and cortisone group. *Double asterisks* significant difference of improvement from 6 to 12 weeks between the ACP and cortisone group. *Triple asterisks* significant difference of improvement from baseline to 12 weeks between the ACP and cortisone group

better after 12 weeks in the ACP group, which was further supported by the finding that the shoulder scores 12 weeks versus 6 weeks and 12 weeks versus baseline were better in the ACP group with statistical significance. However, after 6 months, statistically significant differences between the two groups in terms of shoulder function and MRI findings could not be found anymore.

As hypothesized, subacromial injection of autologous conditioned plasma (ACP) in symptomatic partial rotator cuff tears has a better outcome compared with subacromial injection of cortisone as demonstrated by the 3-month data analysis. However, this difference could not be seen 6 months after injection any more.

Both groups showed a statistically significant better shoulder function after subacromial injection over time.

Cortisone is widely used to treat patients with shoulder pain [29], and there is no doubt about the positive effect on pain especially in the short term [48]. However, the potential complications of corticosteroid injections should also be taken into account, especially for the elderly [48]. Local corticosteroid application may weaken specific regions of the injected tendon and may make it more prone to rupture [18]. This weakening effect manifests itself in the individual collagen fascicles that constitute the tendon [18].

Numerous studies have documented the beneficial effects of individual growth factors on tendon healing in animal models [17, 21, 24, 37, 44]. This was shown for platelet concentrates and other orthobiologics such as autologous processed serum contain factors such as bone morphogenetic proteins, transforming growth factors, and fibroblast growth factors [6, 11, 41]. Application of these agents was shown to promote tendon cell proliferation, collagen synthesis and vascularization in vitro and in vivo [4, 12, 19, 43].

Several authors suggested PRP as an option to treat rotator cuff tendinopathies [10, 26, 30]. Scarpone et al. [42] found significant and sustained improvement in pain, function and MRI outcomes in 19 shoulders within 18 patients with refractory rotator cuff tendinopathy. Rha et al. [35] found better results for PRP injections as compared to dry needling in patients with partial rotator cuff tears or tendinosis.

A beneficial effect was also seen using PRP, platelet leukocyte membrane, platelet-rich fibrin matrix or plasma rich in growth factors in addition to rotator cuff tear surgery [2, 15, 16, 23, 33, 34, 46].

Table 2 Distribution of partial rupture/tendinopathy grade before and after infiltration of ACP or cortisone

Grade	0 (%)	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)
Pre-ACP				76	24	
Post-ACP	5	5	14	38	33	5
Pre-cortisone				68	32	
Post-cortisone			6	53	35	6

On the other hand, Kesikburun et al. [25] found no difference by injecting PRP or saline for treatment of rotator cuff tendinopathy or partial tendon ruptures at a 1-year follow-up. Barber et al. and several other researchers [1–3, 5, 7, 22, 28, 39, 40, 45, 47] found no beneficial effect using PRP during shoulder surgery.

MRI changes in both treatment groups did not show any significant trend. This could indicate that MRI as a follow-up method may lack both the sensitivity and specificity for the types of changes occurring. The literature is controversial and describes improvement [1, 2, 8, 16, 34, 42], no improvement [5, 40, 45, 47] or even deterioration [3] upon platelet concentrate injection.

The rather clear results of this study may due to the fact that a rather small number of physicians and radiologists were involved assessing MRIs and the shoulder scores, that the number of patients included in this study was reasonably high and that the clinical examinations by means of shoulder scoring systems and MRIs scoring systems were strictly standardized.

Another potential advantage of the study was the established close contact to general practitioners and family physicians surrounding the hospital due to the geographic situation of a high mountain valley, thus ensuring that the patients were quite compliant with the treatment regime and with adherence to follow-up visit schedules.

On the other hand, the injections were not controlled by ultrasound, and the exact place of injection except being subacromial could not be checked; in addition, it could not be definitely controlled if the patients did not do any home exercises or gym training by their own, even if they were asked and told not to do so. In addition, the study was done retrospectively and was not blinded or randomized.

This study contributed new data to the discussion about PRP and suggests ACP to be a good alternative to cortisone in treatment of a partial tear of the supraspinatus tendon. This study could not find any evidence on specific changes in the MRI investigations.

Conclusion

This study concludes that subacromial injection with autologous conditioned plasma (ACP) for treatment of a partial tear of the supraspinatus tendon is comparable to the conventional cortisone injections with the potential additional advantage of an earlier benefit 3 months after injection although a statistically significant benefit in outcome parameters could not be demonstrated 6 months after injection any more. Therefore, subacromial ACP injections should be a good alternative to subacromial cortisone injections, especially in patients with contraindication to cortisone.

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

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