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Single injection of platelet-rich plasma (PRP) for the treatment of refractory distal biceps tendonitis: long-term results of a prospective multicenter cohort study

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Abstract

Purpose There is a lack of evidence regarding the use of PRP in the treatment of distal biceps tendonitis. The purpose of this study was to assess the effectiveness of ultrasound (US)-guided injection of PRP in relieving pain and functional impairment in the treatment of refractory distal biceps tendonitis.

Methods Twelve patients from two large tertiary referral hospitals were recruited over a period of 20 months. Clinical diagnosis of distal biceps tendonitis was confirmed using magnetic resonance imaging. All patients had a single US-guided injection of PRP carried out by the two senior authors. Patients were objectively assessed for clinical and functional improvement using visual analogue (VAS) rest and activity pain scores, subjective satisfaction scale, elbow functional assessment (EFA) and isometric muscular (biceps) strength. Symptom severity and subsequent functional outcome were measured pre-injection and at final follow-up.

Results At a median follow-up of 47 months (36–52 months), all patients showed significant improvement in pain ($p < 0.002$) and functional outcome ($p < 0.004$). Median resting VAS score improved from 6 (3–8) to 0.5 (0–2) and the activity VAS score improved from 8 (6–9) to 2.5 (0–4). EFA improved from 63 to 90. In the English cases, isometric muscular strength also showed significant improvement. All patients were satisfied with the clinical and functional outcomes at final follow-up.

Conclusion US-guided PRP injection seems to be an effective treatment modality for symptomatic refractory distal biceps tendonitis.

Level of evidence III.

Keywords PRP · Distal biceps tendonitis · VAS · Functional outcome · Isometric muscular (biceps) strength

Introduction

Acute and chronic musculoskeletal injuries in sports are common and problematic for both athletes and clinicians. These injuries are often difficult to treat, and many patients suffer from decreased performance with persistent pain and discomfort [3, 21, 24]. Although injuries of the distal biceps tendon are rare, this clinical entity is increasingly reported in the medical literature. Injuries are the result of repetitive intrinsic or extrinsic overload, resulting in micro-rupture of the tendon. Distal biceps tendonitis can be considered part of the continuum of the same disease process, the spectrum which includes partial tearing of the distal biceps tendon [12].

To date, conservative treatment options are offered with the assumption that it is a self-limiting condition, like other tendinosis. In our experience distal biceps tendonitis is

This study was conducted according to current GCP and ISO 14155 guidelines.

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difficult to manage with conservative treatment proving frequently non-responsive to rest, activity modification, bracing, physical exercise programmes. Despite the fact that anti-inflammatory agents are frequently used in the treatment of distal biceps tendonitis, the available human histology studies suggest no significant inflammatory role at 4 months. Several animal models indicate that an inflammatory reaction is present in acute situations (first 2 weeks) but a degenerative process soon supersedes [2, 7, 16, 17, 26, 27]. Second-line treatments such as corticosteroid injections give possible concerns relating to tendon integrity post-injection. In (chronic) tendon lesions, there is lack of good evidence to advocate the use of local corticosteroid injections [8, 13, 23]. Surgical treatment is used arbitrarily in few small retrospective cases. Complete detachment of the distal biceps tendon with debridement and re-attachment of the tendon have been successful in alleviating pain. However, with the results of these studies, it is impossible to distinguish between pathologic tendons that will resolve with time or respond to non-surgical treatment and those that require surgical treatment.

Platelet-rich plasma (PRP) is increasingly used in a diverse range of tendinosis [10, 15, 20, 22]. PRP is a bioactive component of whole blood. Upon platelet activation, different bioactive factors are released, which may influence tissue healing through processes including proliferation and differentiation, cellular chemotaxis, angiogenesis, eradication of tissue debris and the laying down of extracellular matrix [1]. According to Mos et al. [6], in vivo application of PRP in tendon injuries promotes angiogenesis and generation of fibrovascular callus and might promote the catabolic demarcation of traumatized tendon matrices. The possible beneficial effect for tendinosis, which are degenerative in nature, remains unanswered. To date, there is lack of evidence to recommend the use of PRP in a diverse range of tendinosis, because trials remain scarce with methodological problems and inconsistent results.

This study evaluated the clinical and functional outcome for US-guided single-shot PRP injection in patients with refractory distal biceps tendonitis from two large tertiary referral hospitals. A prospective study design was used to provide evidence for PRP in the treatment of this rare clinical entity on the long-term.

Materials and methods

A prospective multicenter cohort study of US-guided PRP injection was performed for all patients diagnosed with refractory distal biceps tendonitis. Patients were included in a time-period of 20 months. Eligible for the study were all patients >18-year old with pain unresponsive to one of

three conventional therapy programmes (physical exercise therapy, non-steroidal anti-inflammatory medications and local steroid injections). The exclusion criteria were as follows: pregnancy, systemic diseases such as diabetes, rheumatoid arthritis, hepatitis, coagulation disorders, previous surgery for elbow tendinosis, neurologic disorders, uncooperative patients, steroid injection within the preceding 3 months and complete tendon ruptures (grade 4). This study was conducted according to current GCP and ISO 14155 guidelines. All patients underwent informed consent prior to the participation in this study. Patient selection was conducted in the Wrightington Hospital in the UK and the St. Elisabeth Hospital Tilburg in the Netherlands. The predominant symptom was pain at the insertion of the distal biceps tendon in the radius unrelated to an acute traumatic event. The clinical diagnosis of distal biceps tendonitis was confirmed using magnetic resonance imaging (MRI), which was a valuable tool in differentiating cases where there was sufficient tendinosis or partial tearing of the tendon, usually near or at its attachment site. A classification system was used for grading the severity of tendinosis on MRI. The 4-point classification system can be described as follows: 0; normal tendon, 1; tendinosis of the distal biceps, with high signal and fluid in the tendon sheath, 2; partial tear at the insertion site, 3; partial tear at the musculoskeletal junction, 4; complete rupture. MR imaging of the distal biceps tendon was performed in the axial plane, with the patient's arm extended or with the arm overhead, the elbow flexed to 90°, and the forearm supinated, so that the thumb points superiorly. The acronym FABS, flexed elbow, abducted shoulder, forearm supinated, has been used to describe this imaging technique [4].

The aim of this study was to evaluate the outcomes after a single PRP injection, and additional injections were defined as treatment failure. In the study period, 12 patients were recruited. Two were female, and ten were male patients. The median age at onset of symptoms was 41 years. The median duration of symptoms was 8 months.

Table 1 Baseline demographic data

Baseline characteristics	<i>n</i> = 12
Age years	
Median (range)	41 (28–65)
Gender <i>n</i> (%)	
Male	10 (83)
Female	2 (17)
History of repetitive heavy use of the elbow	
Sport <i>n</i> (%)	8 (67)
Occupation <i>n</i> (%)	4 (33)
Symptom duration (pre-intervention)	
Median months (range)	8 (0.8–36.5)

All patients had a history of repetitive heavy use of the affected elbow either through sport or occupation (Table 1).

US-guided PRP injection

In ten patients, the GPS[®] Recover System (Biomet Biologics, Warsaw, Indiana) was used. This device uses a small centrifuge and disposable cylinders to isolate the platelet- and leucocyte-rich fraction from 27 mL of the patients' blood. Three microlitres of L-PRP was collected for each patient. PRP was buffered to physiological pH with 8.4 % sodium bicarbonate, which yielded an eightfold concentrate platelets of patients own blood. No activating agents were used. Total time from blood aspiration to re-injection of PRP was approximately 30 min. All procedures were carried out in a standard day-case operating theatre in aseptic conditions. In the remaining two patients, different PRP preparation systems were used, in one patient the Caption system[™] and in the other patient the Arthrex ACP[™] was used.

Ultrasound (US)-guided injection was performed with the patient in supine position. At right angles, the probe was placed into the distal biceps tendon, and the needle was inserted parallel to the transducer. Continuous and real-time US images were used to observe the advancement of the needle into the distal tendon. All patients had US-guided PRP injections carried out by the two senior authors (LF & FvB).

Clinical and functional outcome assessment

Data analysis was performed by retrieving data from medical records regarding patient demographics, duration of symptoms, details of previous therapies, type of PRP preparation, complications, recurrences and length of follow-up. Clinical and functional outcome scores were used pre-intervention, and at final follow-up at which times the following were recorded: Visual Analogue Scale (VAS) rest and activity pain scores, subjective satisfaction measured on a scale of 0–100 and elbow functional assessment (EFA) scores. In the English cases, isometric muscular (biceps) strength was assessed using the MICROFET2 hand-held dynamometer (Hoggan Health Industries, Cooper IL.). This device records data in pounds and has been shown to be a valid and reliable measure of isometric strength [5, 9]. Post-treatment regime included eccentric exercises to strengthen the biceps and its tendon.

The Local Medical Ethical Committee and the National and Institutional Review Board approved the study as an amendment to a randomised controlled trial in lateral epicondylitis. This trial is registered with identifier number 2007-004947-31 at <http://www.clinicaltrials.gov>.

Table 2 Pre-operative and post-operative MRI grading the severity of tendinopathy

Study no.	Pre-operative MRI	Post-operative MRI
1	3	n/a
2	1	n/a
3	3	n/a
4	2	n/a
5	1	2
6	2	0
7	2	1
8	1	1
9	2	0
10	3	1
11	1	0
12	3	2

Four-point classification system: 0; normal tendon, 1; tendinopathy of the distal biceps, with high signal and fluid in the tendon sheath, 2; partial tear at the insertion site, 3; partial tear at the musculoskeletal junction, 4; complete rupture

Statistical analysis

This cohort study in two centres should be seen as a pilot study focusing on feasibility and safety of this treatment. A post hoc power analysis with the program G*Power revealed that on the basis of an *n* of 12, the mean and standard deviation of all measures of the pre- and post-scores, the power was higher than the recommended 0.80 level.

A descriptive data analysis is presented for the demographics of the included patients. Data analysis of pre- and post-injection outcome scores was performed using the Wilcoxon Signed-rank test. Statistical analysis was performed by David Nuttall, Medical Statistician, Upper Limb Unit, Wrightington using Statistical Package for the Social Sciences (SPSS, Chicago, Illinois). The level of significance was set at $p < 0.05$.

Results

A total of 12 patients (two female and ten male patients) with refractory distal biceps tendonitis with a median age of 41 years and a median clinical follow-up of 47 months were eligible for final assessment.

On the pre-operative MR imaging, six patients had a partial rupture and two patients had a grade III tear of the distal biceps tendon. In the follow-up period, MRI was only performed in the Dutch cases where two patients had a partial rupture, whereas the other patients showed only signs of tendinosis or had a normal tendon (Table 2). Wilcoxon Signed-rank tests indicated significant improvement in

Table 3 Data analysis of pre- and post-injection outcome scores (Wilcoxon Signed-rank test.)

	Pre-intervention	Final follow-up	<i>p</i> value
VAS-r	6 (3–8)	0.5 (0–2)	<0.002
VAS-a	8 (6–9)	2.5 (0–4)	<0.002
EFA	63 (54–94)	90 (70–100)	<0.004
Biceps strength	14.5 (8–18)	22 (18–24)	

VAS-scores both in rest and during activity and for the EFA. The resting VAS (VAS-r) pain score showed an improvement in median from six pre-treatment to 0.75 post-treatment ($Z = -3.07$, $p = 0.002$). The activity VAS (VAS-a) score improved from a median of eight pre-treatment to a median of 2.5 post-treatment ($Z = -3.08$, $p = 0.002$). The functional assessment score EFA improved from a median of 62.50–90.00 at final follow-up ($Z = -2.85$, $p = 0.004$). In the English cases, isometric muscular strength improved significantly with a 56 % increase (Table 3). There were no adverse events of the interventional procedure and no patients required more than one injection. There were no patients with recurrence of symptoms.

Discussion

Most of the scientific publications involving the use of PRP on human tendons are studies with poor methodological quality [10, 15, 20, 22]. To date, level I evidence only exists for the use of PRP in lateral elbow tendinosis [11, 18, 19].

The present study is the first study to provide evidence for the use of US-guided PRP injection in the treatment of symptomatic refractory distal biceps tendonitis. Major strengths of this study are the long-term follow-up in which we included different grades of tendinosis with overall good results for this method of treatment. Within a prospective study design, the clinical and functional outcome scores are presented from two large tertiary hospitals. At a median follow-up of 47 months (range 36–52 months), all patients showed significant improvement in pain and functional outcome ($p < 0.0001$). All patients were satisfied with the clinical outcomes at final follow-up. No adverse events of PRP injection were reported, nor did any patient report recurrence of symptoms.

Injuries to the tendons of the elbow occur frequently in the overhead athlete, creating a significant loss of function and a challenging dilemma to medical professionals. Distal biceps tendon injuries are uncommon, as illustrated by the small cohort of patients recruited from two large tertiary referral hospitals in our study. There is a paucity of the literature regarding the natural history and treatment of distal biceps tendonitis. Conservative treatment options

are offered with the assumption that, like other tendinosis, it is a self-limiting condition. In our experience, distal biceps tendonitis is difficult to manage with conservative treatment proving frequently non-responsive to rest, splinting, NSAID's and physical exercise programmes, which is reflected by the duration of symptoms before injection with PRP. Distal biceps tendonitis and tendinosis can be considered part of a continuous spectrum of disease with frequently associated partial tearing of the distal biceps tendon [12]. Studies by Kelly et al. and Vardakas et al. [14, 25] showed improvement in elbow function after surgical repair for symptomatic refractory distal biceps tendon tears in small case series. In the analysis of these studies, however, it is impossible to distinguish between pathologic tendons that will resolve with time or respond to non-surgical treatment and those that require surgical treatment. The aim of this study was to provide evidence for the use of PRP in refractory distal biceps tendonitis. Refractory tendonitis was defined as cases in which symptoms were unresponsive to 1 of 3 conventional therapy programmes (physical exercise therapy, non-steroidal anti-inflammatory medications and local steroid injections). The median onset of symptoms was 8 months in our study. Distal biceps tendon disorders may be challenging to identify because of their diverse clinical presentations. In our study, all patients diagnosis was confirmed using a supplementary MRI, where a classification system was used for grading severity of lesion of the distal biceps tendon. US-guided injection was used for PRP injection in our study. An injection of the distal biceps brachii tendon can be more accurately performed using US guidance, because of the inherent difficulty in targeting the distal biceps tendon deep within the antecubital fossa.

In the published medical literature, there is a paucity of evidence for use of PRP in the management of distal biceps tendonitis. Whilst the results of this study are promising, there are some limitations, which warrant consideration. The small number of patients can confound the clinical results; however, the rarity of distal biceps tendinitis as a clinical entity makes it almost impossible to conduct a study with a larger patient cohort. Another weakness of the study is that the study population was not randomised with a control group, thereby failing to exclude a possible placebo effect. A further shortcoming of the study is that the effectiveness of this method of treatment was not evaluated at different time intervals. This would be favourable from a clinical point of view to evaluate the natural history of the condition and the prognosis. The aim of this study was to evaluate the outcomes after a single PRP injection, and additional injections were defined as treatment failure. This also can be a factor, which can influence the outcome. A randomized controlled trial comparing outcomes for PRP and surgical debridement and reattachment would also be desirable. Whilst it is accepted that complete ruptures of

the distal biceps in selected patients does well with anatomic repair, the literature is scarce regarding treatment of partial tears [14, 25].

Conclusion

This is the first study in a prospective multicenter design to provide evidence for the use of PRP in refractory distal biceps tendonitis. All patients showed a significant improvement in VAS rest and activity scores with subsequent improvements in EFA and high subjective satisfaction at final follow-up. US-guided PRP injection seems to be an effective treatment modality for symptomatic refractory distal biceps tendonitis.

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