Journal of Orthopaedics 15 (2018) 239–241

Contents lists available at ScienceDirect

Journal of Orthopaedics

journal homepage: www.elsevier.com/locate/jor

Platelet rich plasma injections for lateral epicondylitis of the elbow reduce the need for surgical intervention

Graham Hastie*, Mazen Soufi, James Wilson, Bibhas Roy

Central Manchester University Hospitals NHS Trust, Trafford General Hospital, Moorside Road, Manchester M41 5SL, United Kingdom

ARTICLE INFO

Keywords:
Platelet rich plasma
Tennis elbow

ABSTRACT

Objective: We aimed to assess the effectiveness of PRP injections in lateral epicondylitis of the elbow as it was felt after PRP introduction the numbers of patients requiring surgery for had reduced.

Methods: We conducted a retrospective review of cases from the 1st January 2008 to 31st December 2015. The numbers of patients undergoing surgical release and the numbers of patients requiring PRP injections were recorded each year and the numbers of patients requiring surgery was compared pre and post PRP injection to ascertain if PRP introduction reduced surgical intervention.

Results: Prior to PRP, a yearly mean of 12.75 patients underwent surgery, since PRP this reduced to 4.25 patients, $P < 0.001$. This leads to an absolute risk reduction of 0.773 and number needed to treat of 1.3. PRP injection successfully reduced symptoms in 56/64 (87.5%) patients in our study.

Conclusion: We consider PRP injection, for intractable lateral epicondylitis of the elbow, not only a safe but also very effective tool in reducing symptoms and have shown it has reduced the need for surgical intervention in this difficult cohort of patients.

1. Introduction

Lateral epicondylitis, also known as 'tennis elbow,' is a degenerative disorder of the common extensor origin of the lateral humeral epicondyle. The prevalence in the general population has been widely reported to range from 1% to 3% with a peak prevalence in the fifth decade.[1,2] It is often associated with jobs which involve manual work and vibrating tools[3] and despite the name of the condition it is rarely associated with playing tennis.[1]

The lateral epicondyle is the common origin of five extensor muscles in the forearm and the suggested pathogenesis is of overload injury and repetitive microtrauma.[4] Rather than being a purely inflammatory condition it is suggested that there is an initial inflammatory response which is followed by degenerative changes with production of disorganised collagen which can then lead to structural failure/tearing of the tendon origin.[5]

The mainstay of treatment is non-operative and includes watchful waiting, physiotherapy, activity modification, bracing, nonsteroidal anti-inflammatory drugs, and injections.[4] There is a subgroup of patients however who do not respond to non-operative measures and require operative intervention.

Multiple injectables have been tried and historically the mainstay of treatment was corticosteroid injections but more recently platelet rich plasma (PRP), autologous whole blood and botulinum toxin have all been used.[1] Corticosteroid injections have been shown to give good short term pain relief, however their long term consequence may actually be tendon degeneration.[6] Gautam et al used ultrasound to assess the common extensor origin 6 months after corticosteroid injection and found reduced thickness of the tendon with increased cortical erosions in the lateral epicondyle suggesting further degeneration.[6]

PRP and autologous whole blood have been shown to give long term improvements in patient symptoms in multiple studies[7–10] with some suggesting that PRP may have a slightly more beneficial affect that autologous whole blood.[7,11] Studies have shown that PRP is superior to corticosteroids in terms of improving patient symptoms[3] and Gautam et al also showed tendon regeneration, in the form of improved thickness of the tendon, increase in the vascularity and improved tendon morphology on ultrasound scans.[6]

There is some controversy in the literature however as there are studies which have stated PRP/autologous whole blood injections not only have no benefits over corticosteroids but go as far as to say there is 'strong evidence that PRP injections are not efficacious in the management of chronic lateral elbow tendinopathy'.[4,12]

Finally there is controversy with regards to the differing types of PRP available, either leukocyte rich PRP (L-PRP) or PRP in which leukocytes have specifically been eliminated, pure PRP (P-PRP). L-PRP

* Corresponding author.
E-mail address: grhastie@doctors.org.uk (G. Hastie).

https://doi.org/10.1016/j.jor.2018.01.046
Received 18 July 2017; Accepted 14 January 2018
Available online 31 January 2018

has shown significant improvements in the literature with regards to pain relief and increase in function when compared to either corticosteroids,[13] local anaesthetic[14] or control groups.[15] It has even been suggested that due to these improvements L-PRP "should be considered prior to surgical intervention".[14]

In our institution prior to 2012 PRP injections were not available and patients were treated with other conservative measures. If they had recurrent or intractable symptoms for a prolonged period they were offered surgery. After 2012 patients were offered PRP injections and there was a general feeling that this has reduced the numbers of patients requiring surgical intervention. Our aim was to conduct a retrospective review of prospectively collected data to assess whether the introduction of PRP injections for lateral epicondylitis led to a reduction in patients subsequently undergoing surgical release.

2. Methods

A complete data set of all arthroscopic lateral release procedures performed by the lead author (BR) at our institution was identified from electronic patient records. The period identified for the study was from the 1st January 2008 to 31st December 2015. The records of each patient were the reviewed, including evaluation of the operation note to review indications for the procedure. Most patients had their diagnosis confirmed via magnetic resonance imaging (MRI) scanning and these were graded from 1 to 3; 1 – minor tendon oedema/thickening; 2 – intermediate thicking/focal signal increase; 3 – partial/full thickness tears. Prior to 2012 PRP injections were not available and patients not responding to conservative measures were treated with surgery. After 2012 patients with symptoms intractable to conservative measures were offered PRP injection at the stage surgery would have previously been offered. Patient outcomes with regards to improvement following surgery were also recorded. The numbers of patients undergoing release and the numbers of patients requiring PRP injections were recorded each year and the numbers of patients requiring surgery was compared pre and post PRP injection using a Chi squared test. Absolute risk ratio (ARR) and number needed to treat (NNT) were also calculated.

The surgical technique used for arthroscopic release was as described below.

The elbow joint was distended with saline and two standard arthroscopic portals were used. The proximal anteromedial portal was 2 cm proximal and 2 cm anterior to the medial epicondyle and the proximal lateral portal 2 cm proximal and 2 cm anterior to the lateral epicondyle. Using the proximal anteromedial portal the capsule is removed from the intra-articular aspect revealing the ECRB tendon, which was followed up to its insertion on the lateral epicondyle. The ECRB was debrided without causing damage to the lateral ulnar collateral ligament.

The technique of PRP injection is as follows. The procedure is performed with the Gravitational platelet separation system (GPS®III) from Biomet, Warsaw, Indiana. 54 mL of blood is collected using a 60 mL syringe containing 6 mL of citrate anticoagulant. This is transferred to the GPS®III separation tube that uses centrifugal force to separate and 'trap' the platelet rich layer. Typically, 6 mL of platelet rich plasma is obtained, which is the of the L-PRP type, although no cell counts were taken in this study. This is then buffered with 8.4% sodium bicarbonate following manufacturer instructions. The injection is performed using a 22 g needle. A single skin entry is made over the lateral epicondyle over the maximal tender area. Three separate stabs are subsequently made into the common extensor tendons with about 2 mL injected at each site. Resulting ECRB/Common extensor spasm is often noted from involuntary middle finger extension (See Fig. 1).

3. Results

In the four years prior to the introduction of PRP injections, 2008–2012, there were 52 patients who underwent arthroscopic release for tennis elbow, with a mean of 12.75 patients a year. In the four years after PRP introduction, 2012–2015, this number reduced to 17, with a mean of 4.25 patients a year. Using a Pearsons chi squared test this is a significant fall in the number of arthroscopic releases for tennis elbow required, $P < 0.001$.

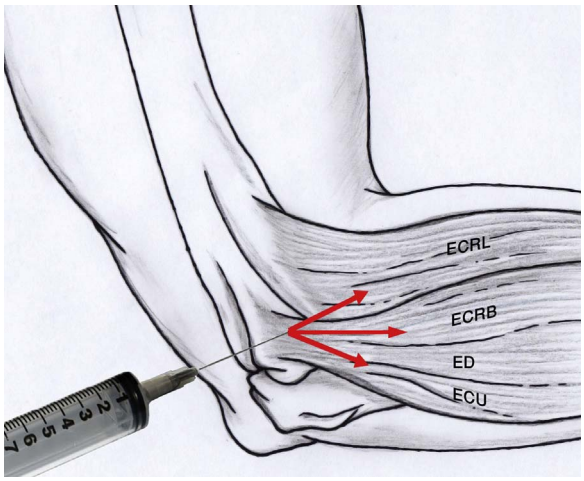

Fig. 1. Injection technique of PRP.

On review of the clinic and operative notes it is clear that the indications for intervention have not changed. Prior to 2012 patients were offered release if they had a clinical diagnosis of tennis elbow with symptoms for over 6 months, and had tried non-operative methods of relief, including physiotherapy and activity modification. We did not offer steroid injections but some had already tried these without relief at the GP. Since 2012 these same indications have led to PRP injection and only if this failed, or patients refused the injection, were they offered surgical treatment. We considered that without the PRP all of the patients with intractable symptoms after 2012 previously would have progressed to surgical intervention as conservative treatments had failed. MRI to confirm the diagnosis was performed in 60 out of 64 patients having PRP (94%) and 54 out of 69 (78%) patients undergoing surgical release. Of the 60 PRP patients with MR imaging 10 had grade 1 changes, 25 grade 2 and 25 grade 3. Of the 54 patients who had surgery and MR imaging 7 had grade 1 changes, 21 had grade 2 changes and 26 had grade 3 changes.

Since 2012 64 patients have undergone PRP injection with only 8 progressing on to arthroscopic release, of these no patients had grade 1 changes, 4 had grade 2 changes and 4 had grade 3 changes on MR imaging. The other 9 who have undergone surgery since PRP introduction refused the injection and requested surgery either due to a successful outcome from surgery on their other arm or due to their beliefs. This significant reduction in patients requiring surgery since PRP introduction leads to an absolute risk reduction of 0.773 and number needed to treat on 'as-treated' basis of only 1.3.

4. Discussion

Lateral epicondylitis will continue to be a relatively common disorder with a significant health burden.[2] As well as PRP injection and corticosteroids, described above, other treatments such as, Botulinum toxin A, have been used to treat the epicondylitis. Botulinum toxin A works by blocking acetylcholine receptors causing temporary paralysis within the muscle. It is suggested this reversible paralysis stops further microtrauma and gives the tendon time to heal. Although pain scores are improved however there are some complications to its use however with weakness to wrist extensors and decreased grip strength common side effects.[5]

It is known however that in patients not responding to these measures, and where symptoms have been present for longer than six

months, surgical intervention is likely to be required to resolve the symptoms.[2] The surgical intervention used is either an open or arthroscopic release of the common tendon origin but should not be taken lightly as although surgery can produces a good outcome in terms of pain relief and function the rehabilitation period and postoperative recovery can be up to 6 months.[16] Elbow arthroscopy is also not a procedure without risk and has been shown to have an overall complication rate of 14% with major complications requiring further surgery at 5%.[17] Previously neurovascular injury was a main concern following elbow arthroscopy however more recent studies have shown newer techniques have reduced this risk significantly.[18,19] This would not detract from the fact however that surgery for lateral epicondylitis would also have a significant cost implications. With complex tariff payment systems within the NHS it is difficult to place an exact figure on procedural costs but with added equipment and theatre time compared to injection it is likely to be significantly higher.

Our results add to the growing evidence that PRP injections can give long-term improvement in symptoms to patients with previously intractable lateral epicondylitis. We hypothesise that this improvement is likely to come from growth factors present in the PRP injection. Platelets have been shown to contain growth factors such as; platelet derived growth factor (PDGF); transforming growth factor (TGF)-β; insulin-like growth factor (IGF); epidermal growth factor (EGF); vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF).[20] These factors are released from the alpha granules after injury and bind of target cells (e.g. mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells). These receptors activate an intracellular signal protein that causes the expression of a gene sequence that then directs cellular proliferation, matrix formation, osteoid production or collagen synthesis dependent on the cell activated.[21] Specifically with regards to tendon damage/healing in lateral epicondylitis PRP injection would increases collagen production and cell viability and stimulate angiogenesis due to the release of the above factors.[20] This could explain the findings of Gautam et al who showed not only improvement in symptoms following PRP injection but also increase in tendon thickness/vascularity.[6] With regards to the differences in L-PRP, used in this study, and P-PRP it has been hypothesized that the leucocytes in L-PRP create an antibacterial response and debride the dead tissue allowing the tendon to regenerate using the above growth factors.[13]

Our study adds to the evidence that PRP injection for intractable lateral epicondylitis of the elbow is an acceptable and useful treatment with improvement in symptoms in 56 out of 64 patients (87.5%). It adds to the literature in that we have tried to ascertain the effect of PRP on reducing the need for a complex, risk laden, surgical intervention by estimating the number of PRP injections required to avoid one surgery, NNT 1.3.

This was a retrospective as opposed to a prospective study and sampling errors may be present due to selection bias. Patients offered PRP injections may have been more prepared to accept the treatment when compared to patients offered surgery as the procedure carries relatively less risk and therefore not all the patients treated with PRP may have opted for surgical intervention. This may mean that due to our NNT being based on an intention to treat basis the figure of 1.3 may be slightly lower than the true value. In the PRP group, progress to surgery was detected from health care records at our institution. This may have introduced limitations as patients may have been treated in other institutions after improvement and discharge from our clinic. Further studies with better control of the variables in the setting of a randomised control trial are needed to confirm our findings. To our knowledge there has never been a randomised control trial comparing PRP injection and surgery as a treatment for lateral epicondylitis of the elbow.

In conclusion we consider PRP injection, for intractable lateral epicondylitis of the elbow, not only a safe but also very effective tool in reducing symptoms and have shown it has reduced the need for surgical intervention in this difficult cohort of patients.

Conflicts of interest

None.

References

1. Tosti R, Jennings J, Sewards JM. Lateral epicondylitis of the elbow. *Am J Med.* 2013;126(4):357 [Internet]. Elsevier Inc. e1–357. e6.
2. Sanders Jr T, Kremers HM, Bryan AJ, Ransom J, Smith J, Morrey B. The epidemiology and healthcare burden of tennis elbow: a population based study. *Am J Sports Med.* 2015;43(5):1066–1071.
3. Yadav R, Kothari SY, Borah D. Comparison of local injection of platelet rich plasma and corticosteroids in the treatment of lateral epicondylitis of humerus. *J Clin Diagn Res.* 2015;9(October):2014–2016 [Internet].
4. Krogh TP, Fredberg U, Stengaard-Pedersen K, Christensen R, Jensen P, Ellingsen T. Treatment of lateral epicondylitis with platelet-rich plasma, glucocorticoid, or saline: a randomized, double-blind, placebo-controlled trial. *Am J Sports Med.* 2013;41(3):625–635 [Internet].
5. Kahlenberg CA, Knesek M, Terry MA. New developments in the use of biologics and other modalities in the management of lateral epicondylitis. *Biomed Res Int.* 2015;2015:439309 [Internet]. Hindawi Publishing Corporation.
6. Gautam VK, Verma S, Batra S, Bhatnagar N, Arora S. Platelet-rich plasma versus corticosteroid injection for recalcitrant lateral epicondylitis: clinical and ultrasonographic evaluation. *J Orthop Surg (Hong Kong).* 2015;23(1):1–5 [Internet].
7. Creaney L, Wallace A, Curtis M, Connell D. Growth factor-based therapies provide additional benefit beyond physical therapy in resistant elbow tendinopathy: a prospective, single-blind, randomised trial of autologous blood injections versus platelet-rich plasma injections. *Br J Sports Med.* 2011;45(12):966–971.
8. Murray DJ, Javed S, Jain N, Kemp S, Watts AC. Platelet-rich-plasma injections in treating lateral epicondylosis: a review of the recent evidence. *J Hand Microsurg.* 2015;7(2):320–325 [Internet].
9. Behera P, Dhillon M, Aggarwal S, Marwaha N, Prakash M. Leukocyte-poor platelet-rich plasma versus bupivacaine for recalcitrant lateral epicondylar tendinopathy. *J Orthop Surg (Hong Kong).* 2015;23(1):6–10 [Internet].
10. Ahmad Z, Brooks R, Kang SN, et al. The effect of platelet-rich plasma on clinical outcomes in lateral epicondylitis. *Arthrosc—J Arthrosc Relat Surg.* 2013;29(11):1851–1862 [Internet] Arthroscopy Association of North America.
11. Raeissadat SA, Sedighipour L, Rayegani SM, Bahrami MH, Bayat M, Rahimi R. Effect of platelet-rich plasma (PRP) versus autologous whole blood on pain and function improvement in tennis elbow: a randomized clinical trial. *Pain Res Treat.* 2014;2014 [Hindawi Publishing Corporation].
12. De Vos R-J, Windt J, Weir A. Strong evidence against platelet-rich plasma injections for chronic lateral epicondylar tendinopathy: a systematic review. *Br J Sport Med.* 2014;48:952–956.
13. Gosens T, Peerbooms JC, Van Laar W, den Oudsten BL. Ongoing positive effect of platelet-rich plasma versus corticosteroid injection in lateral epicondylitis a double-blind randomized controlled trial with 2-year follow-up. *Am J Sports Med.* 2011;39(6):1200–1208.
14. Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med.* 2006;34(11):1774–1778.
15. Mishra AK, Skrepnik NV, Edwards SG, et al. Efficacy of platelet-rich plasma for chronic tennis elbow controlled trial of 230 patients. *Am J Sports Med.* 2013;42(2):463–471.
16. Oki G, Iba K, Sasaki K, Yamashita T, Wada T. Time to functional recovery after arthroscopic surgery for tennis elbow. *J Shoulder Elb Surg.* 2014;23(10):1527–1531. http://dx.doi.org/10.1016/j.jse.2014.05.010. [Internet]. Elsevier Ltd; Available from.
17. Nelson GN, Wu T, Galatz LM, Yamaguchi K, Keener JD. Elbow arthroscopy: early complications and associated risk factors. *J Shoulder Elb Surg.* 2014;23(2):273–278 [Internet]. Elsevier Ltd.
18. Cefo I, Eygendaal D. Arthroscopic arthrolysis for posttraumatic elbow stiffness. *J Shoulder Elb Surg.* 2011;20(3):434–439.
19. Elfeddali R, Schreuder MHE, Eygendaal D. Arthroscopic elbow surgery, is it safe? *J Shoulder Elb Surg.* 2013;22(5):647–652 [Internet] Elsevier Ltd.
20. de Mos M, van der Windt A, Jahr H, et al. Can platelet-rich plasma enhance tendon repair? A cell culture study. *Am J Sports Med.* 2008;36(6):1171–1178.
21. Pietrzak WS, Eppley BL. Platelet rich plasma: biology and new technology. *J Craniofac Surg.* 2005;16(6):1043–1054.