A Critical Review of the use of Platelet Rich Plasma Injection in the Management of Patella-femoral Syndrome and its use in University Hospitals of Morecambe Bay Trust

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INTRODUCTION

One of the most common musculo-skeletal disorders, anterior knee pain, often referred to as 'jumper's knee', patella-femoral syndrome (PFS) or patella-femoral pain syndrome (PFPS), affects approximately 21-45% of young adults and 15-33% of active adults.¹ The number of treatments available for PFS has expanded over the past 30 years with none proving to be highly successful.² First used in 2014 as a treatment for Patella-femoral Syndrome in the University Hospitals of Morecambe Bay Trust (UHMB), platelet rich plasma (PRP) injection has been performed for a number of years elsewhere for the treatment of acute ligament injuries, chronic tendon injuries and Patella-femoral Syndrome in particular. This critical review will evaluate the evidence base and continued use of PRP injections for PFS as well as comment on its continued use within the Trust.

AIMS

The aims of this critical review are as follows:

1. To review the pathophysiology of Patella-femoral Syndrome (PFS)
2. To review the history and use of PRP injections
3. To explore the scientific rationale behind the use of PRP injections in the treatment of PFS.
4. To analyse and discuss the current evidence base regarding the effectiveness of treating Patella-femoral syndrome with PRP injection.
5. To discuss the suitability of its continued use by practitioners and within the University Hospitals of Morecambe Bay Trust

ANATOMY

The patella is attached anteriorly to the leg via the quadriceps tendon formed by the insertion of the four muscles of the anterior (extensor) compartment of the leg; rectus femoris, vastus lateralis, vastus medialis and vastus intermedius. The patella is attached to the tibia anteriorly via the patella tendon (see figure 1).³ During flexion and extension of the knee the patella glides over the trochlear (also called the patellofemoral groove), a groove found antero-medially between the medial and lateral femoral condyles (see figure 2).

PLATELETS AND PLATELET RICH PLASMA INJECTIONS

Blood consists of blood cells and plasma. Plasma is constituted mostly of water along with platelets and transports blood cells throughout the body.⁵ Derived from the fragmentation of a megakaryocyte, platelets contain no nucleus and their main function is to assist in haemostasis. Within platelet-rich-plasma there are a vast number of growth factors including platelet-derived growth factor (PDGF), insulin-like growth factor (IGF) and epidermal growth factor (EGF) to name but a few.⁶ There are also chemical mediators and cytokines contained within platelets including fibrinogen, von Willebrand factor and histamine.⁶ Growth factors have been demonstrated to promote cell differentiation, proliferation and migration as well as promote angiogenesis.⁷ All of these processes have a role in promoting the restoration of normal tissue architecture and function.⁷

A platelet rich plasma injection (PRP) was first used in 1987 during an open heart surgery procedure but it has only been in the past decade that the use of PRP injection has gained popularity.⁷ It is now used throughout a number of specialities including maxillo-facial surgery, neurosurgery, orthopaedics and sports medicine in particular.⁷ A PRP injection can be prepared in theatres or even outpatient clinics. Using an aseptic approach, the injection is prepared firstly by performing venepuncture on the patient to gather a sample of blood. This sample is then centrifuged to create a minimum concentration of 1,000,000 platelets per microliter in 5 millilitres of plasma which works out at between a 3 to 5 fold increase in the concentration of platelets compared to a normal sample of the patients' blood.⁷ Following an injection of local anaesthetic, the PRP is then injected into the affected area with or without ultrasound guidance (the patellar tendon in patella-femoral syndrome). The clinical rationale is based on reversing the normal blood concentration found in a typical haematoma by increasing the percentage of platelets to approximately 94% and decreasing the less useful red blood cell percentage to approximately 5%.⁸

Within sports medicine, PRP injection is now being used for the treatment of a number of conditions including improving the healing of meniscal and muscle injuries, pain reduction in arthritic knees, stimulation of healing of anterior cruciate ligament injuries and to reduce pain in chronic tendinopathies.⁸ PRP injection has expanded particularly quickly amongst elite athletes with the aim of returning to sport as quickly as possible with minimal intervention required.² It is currently viewed as a controversial intervention within sports medicine due to it often being negatively associated with blood product manipulation, a practice banned within sport.⁹

PATELLA-FEMORAL SYNDROME

Patella-femoral syndrome, also commonly referred to as 'Jumper's Knee', presents with anterior knee pain specifically located at the patella-femoral joint.^{10, 11} The patella-femoral joint is commonly stressed day-to-day when the knee becomes flexed under a load, for example, when going down the stairs or squatting.¹¹ The mechanics of the patella-femoral joint lead to it having to take and

withstand up to seven times the patient's bodyweight when it is loaded in flexion.¹¹ This creates a vast amount of stress that the joint is then exposed to.¹¹

The patient will often describe the pain as being felt around the knee cap or at the lower pole of the patella.^{10, 11} They will often indicate the site of pain by pointing or rubbing over their knee cap.¹¹ In some cases the pain can be so bad that patients can no longer partake in their sport of choice and they may even struggle to sit with their knees bent and in severe cases, ascend and descend stairs.^{12, 11} It is a debilitating condition with one study with a 15 year follow up finding 53% of patients had had to end their sporting career.¹³

The exact aetiology of patella-femoral syndrome remains a debated topic. The international Patello-femoral study group suggest the complex mechanics of the patella-femoral joint provide a stumbling block to the lack of understanding of the syndrome, along with the lack of correlation of symptoms with findings on both X-ray and MRI.¹⁴ Despite this, there have been advancements with a number of theories, some better received than others, now proposed to explain the aetiology and pathophysiology.

Until the 1970s Patella-femoral Syndrome was thought to be related to chondromalacia patellae where there is damage to the posterior cartilage of the knee.¹ Since then a number of theories have proposed a pathophysiology including patella-femoral malalignment (PFM), the tissue homeostasis theory where the loss of osseous and soft tissue of the peripatellar region is the main contributor and a vascular cause leading to repeated episodes of ischemia.¹ What is generally accepted is that overuse and overloading are deemed to be common contributing factors.¹⁵ As mentioned previously, there are also an agreed number of underlying causes including excess sporting activities, joint hypermobility, repetitive trauma and reduced strength of the quadriceps muscles.¹⁵

Important to note is that the mechanism of disease in Patella-femoral Syndrome is classed as a degenerative tendinopathy as opposed to an inflammatory tendinitis, despite an acute inflammatory phase to begin with.^{14, 7} Analysed tissue samples have shown an absence of inflammatory cells in tissue excised from the patellar tendons of patients presenting with acute symptoms.¹⁴ It can be clinically classified into stages with stage 1 presenting as the presence of pain after activity with no functional impairment and stage 4 presenting as complete tendon rupture.¹⁴ On an MRI scan an increase in signal intensity is seen, characteristic of Patella-femoral Syndrome, often accompanied by oedema (see figure 3).⁷

When considering treatment for Patella-femoral Syndrome it is important to distinguish between the acute inflammatory phase against the ensuing chronic degenerative tendon changes.⁷ Currently, treatments for Patella-femoral Syndrome depend on the phase of the condition and consist of resting the knee, strengthening the quadriceps muscles, non-steroidal-anti-inflammatory drugs (despite the absence of inflammatory cells in tendinopathies) and even ultrasound therapy.⁷ Unfortunately, all of the above have a variable success rate with NSAIDs in particular providing a success rate (in general tendon injuries) of just 65%.²

With regards to PRP injection as a method of treatment, it is a relatively new intervention and began

Figure 3: Increased Signal Intensity at Proximal Patella Tendon¹⁶

to be used in orthopaedics in 2003 for management of cartilage problems.² Since then its use has accelerated, particularly within sports medicine amongst elite athletes in the hope of decreasing recovery time and making a faster return to sport.⁷ PRP injection has since been advocated for use in Patella-femoral Syndrome once conservative management options have been attempted with little or no effect on the patient's patella-femoral pain.⁷

ANALYSIS AND DISCUSSION OF THE EVIDENCE BASE FOR THE USE OF PRP INJECTION IN MANAGING PATELLA-FEMORAL SYNDROME

A case-based study conducted by Kon et al in 2009 involving 20 participants found that, in the short-term, patella-femoral pain was reduced following PRP injection and the majority were able to return to full tendon-loading activities.⁹ In this study 3 separate PRP injections into the patella tendon were performed over a period of 45 days with a 15 day gap between each.⁹ A statistically significant improvement in scores including quality of life and knee function were also observed at a 6 month follow up perhaps suggesting a long as well as short-term benefit of PRP injection in patella-femoral syndrome.⁹ Despite this, the authors recognise that longer-term randomised controlled trials are required to further assess these results as well as provide evidence suggesting a long-term benefit of PRP injection.⁹

Another case-based study conducted by Vertrano et al comparing PRP injection for the treatment of Patella-femoral Syndrome to ultrasound shockwave therapy found a statistically significant difference between the two at 6 and 12 month follow up with PRP injection providing more favourable results.¹⁷ At the 12 month follow up 91.3% of patients who received PRP injections declared satisfactory results compared to 60.8% of those who received ultrasound therapy.¹⁷ This case-study could be used as evidence to suggest a long-term benefit of the use of PRP injection in Patella-femoral Syndrome, contrary to Kon's findings.⁹ However, the small sample size of 23 cases in each group limits the external validity and decreases the power of the study. Again this was a case-based study where the authors acknowledge a lack of available randomised controlled trials on the topic.¹⁷

A prospective cohort study conducted in 2012 measuring the effectiveness of PRP injections in treating pain and increasing sporting ability in Patella-femoral Syndrome found statistically significant results in favour of using PRP injection.¹⁸ Pre-PRP injection, 5.6% of patients declared no pain when playing sport for up to 40 minutes.¹⁸ Following the PRP injection this had increased to 22%, providing evidence that PRP injection could well be a short-term solution to Patella-femoral Pain Syndrome.¹⁸ Despite these findings this study was yet again case-based and included 36 patients, a limited sample size.¹⁸ The study also notes that the improvement was only seen in cases who had not received previous treatment including surgery.¹⁸

Fortunately, a randomised controlled trial was conducted in 2014 which compared the use of ultrasound guided PRP injection in Patella-femoral Syndrome to dry needle injection.¹⁹ This study found a marked improvement in score at 12 weeks in the group who received a PRP injection using the Victorian Institute of Sports Assessment (VISA) score for patella tendinopathy.¹⁹ The study subsequently concluded that PRP injection therapy, combined with an exercise regime accelerated the recovery of patella tendinopathy.¹⁹ However, at 26 weeks the difference between the two groups was found not to be statistically significant, again perhaps suggesting that PRP injection has a limited time-period of effect.¹⁹ In fact, the study concludes that the effect of PRP injection in the treatment of patella-femoral syndrome does decrease over time.¹⁹

THE USE OF PRP INJECTION FOR PATELLA-FEMORAL SYNDROME WITHIN THE UHMB TRUST

The current evidence base discussed does seem to suggest a favourable outcome in both pain and sporting ability in patients with patella-femoral syndrome treated with PRP injection. Of the studies noted above, all provided statistically significant evidence that PRP injection improved pain and, when applicable, sporting ability, in some cases with the randomised controlled trial conducted in 2014 in particular providing substantial weight to this claim. Bearing the collation of these findings in mind, it could be proposed that PRP injection for the treatment of patella-femoral syndrome be continued within the Trust.

To improve outcomes, a number of studies recommend that when possible, PRP injection into the patella tendon should be performed with ultrasound guidance, particularly Engebretsen et al.² This allows the exact site of pathology to be identified and treated with PRP therapy proposed to work at its best when injected as close to the site of pathology as possible.²

It should be noted that, as discussed previously, evidence is still lacking on the long-term effects of PRP injection for Patella-femoral Syndrome and this is acknowledged by the authors of most studies. The Trust may wish to take account of this and perhaps consider

following up and auditing the outcomes of patients treated with this intervention within the Trust at specific time intervals such as 3, 6 and 12 months.

Finally, the Trust should remain vigilant for new randomised controlled trials demonstrating statistically significant results of using PRP injection for patella-femoral syndrome. Currently the evidence base remains thin and any addition to this would be welcomed to justify the continued and possible expansion of use of this intervention. Furthermore, there are currently a variety of different methods and techniques of preparing and administering PRP injection therapy with no evidence to support one over another.² The trust should also be encouraged to observe developments in this area with the view to finding the most economically feasible method with the largest evidence base behind it.

CONCLUSION

It is apparent that currently there is a significant lack of research, particularly randomised controlled trials, on the use and results of PRP injection in managing Patella-femoral Syndrome.⁹ Those that are available lack quality surrounding their methodology and cannot be used to justify evidence-based decision making.² This is intriguing and possibly even worrying considering how often it is currently used within sports medicine for tendon injuries and its expansion of use in an outpatient setting.²

With regards to the Trust, there are no guidelines on PRP therapy available to follow at the time of writing.² Using the limited evidence base, the Trust will have to decide (perhaps aided by following up patients via case-study as suggested earlier) whether the available results are convincing enough to continue to provide such a treatment despite its relatively low costs in a condition that is notoriously difficult to treat.

What is becoming clear from the available evidence so far is that PRP injection therapy not only has the potential but also has been shown to improve patient's patella-femoral symptoms including pain. However, a larger evidence base is required to expand the literature and allow practitioners to make a more informed decision regarding their use of this still somewhat controversial treatment.

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