

## Priorities Forum Statement

<b>Number</b>	<b>75</b>
<b>Subject</b>	<b>Autologous Blood and Platelet-Rich Plasma Injection in Tendinopathy</b>
<b>Date of decision</b>	<b>February 2017</b>
<b>Date refreshed</b>	<b>February 2017</b>
<b>Date of review</b>	<b>February 2020</b>

### GUIDANCE

#### **Recommendation: Not routinely funded**

#### **Evidence review**

Tendinopathy is a broad term used to refer to many conditions affecting tendons. They are a common presenting complaint in the primary care and orthopaedic/rheumatology clinic settings. Patients generally complain of pain, often when performing a specific movement. Generally single tendons are affected in the absence of underlying soft tissue disease. Common examples include Achilles tendonitis and lateral epicondylitis (tennis elbow). Such injuries are generally caused by repetitive movements of the joint in the same plane, although tennis only causes around 5% of its eponymous elbow injury<sup>1</sup>. People in occupations involving strenuous manual work are known to be at increased risk, with up to half of cases occurring in mechanics.

Whereas these conditions had traditionally been treated conservatively or with steroid injections, more recently there has been an increase in the number of autologous blood injections carried out. At times these involve the blood first being centrifuged to produce a platelet-rich component which is used for the procedure (Platelet-Rich Plasma – PRP). It is thought that injection of autologous blood provides a dose of growth factors which enhance healing in the affected tendon<sup>1</sup>. By spinning down the blood and selectively injecting the platelet-rich portion, it is thought that a higher concentration of platelet-derived growth factors can be achieved in the target area. The procedure involves taking up to 10ml of blood from a patient into a tube containing clotting inhibitors. This is then centrifuged to extract the platelet and plasma layers. ~2ml is then injected directly into the affected tendon. In cases where whole blood is being used, approximately 5ml is venesectioned into clotting inhibitor as above then injected unprocessed into the tendon<sup>2</sup>.

We will consider a number of trials and reviews considering the potential efficacy of the procedures in the treatment of tendinopathies at different anatomical sites, and also look at comparisons between injections of autologous whole blood versus platelet-rich plasma.

#### **Use in elbow conditions**

A Cochrane review of the use of autologous blood and platelet-rich plasma in lateral elbow pain is pending<sup>2</sup>.

A trial comparing a single injection of either autologous blood or steroid in cases of tennis elbow found that there was no difference in either pain or Nirschl stage (a pain-based measure

of the functional impact of lateral epicondylitis) at 2 weeks post procedure, but did find a significant improvement at 6 weeks follow-up in the blood group compared to the steroid group in both Visual Assessment of Pain scores (VAS) and Nirschl stage (P-values 0.00456 and 0.0396 respectively)<sup>3</sup>.

A 2012 randomised control trial again compared the efficacy of autologous blood injection to corticosteroid injection in lateral epicondylitis<sup>4</sup>. They initially found a statistically significant decrease in both VAS and Nirschl scale measures of pain at 1 week and 4 weeks in the corticosteroid group compared to the blood group. However, they also showed that over a longer time period (12 week and 6 month follow-ups) that the blood group then had decreased pain scores compared to the steroid group. At the final 6 month follow-up, 90% of the blood group had been complete resolution of their pain compared to 47% of the steroid group.

Contrary to the findings in these two papers, a recent study comparing ultrasound guided injection of conditioned autologous plasma to placebo found no significant difference in the pain scores between the two groups when compared at 6 months<sup>5</sup>.

A 2016 systematic review and meta-analysis comparing platelet-rich plasma, autologous whole blood and steroid injections in lateral epicondylitis<sup>17</sup> concluded the differences between the treatments vary depending on the outcome measure used. When looking at pain scores (VAS) 2 months post-treatment, platelet-rich plasma injections had the best outcomes of the three interventions tested. However, if disability scores (DASH, PRTEE) or increased pressure threshold were used then whole blood injections came out as the best treatment both at and after 2 months.

### **Use in knee conditions**

Research into the treatment of patellar tendinopathy generally revolves around athletes, as this group is both at higher risk of the condition and can also be more affected by its presence. The use of platelet-rich plasma was investigated in a 2012 paper specifically looking at ultrasound-guided injections into the patellar and Achilles tendons<sup>6</sup>. Sadly this paper had no control group and as such is of questionable value given the nature of these conditions to improve over time with or without treatment<sup>1, 7</sup>. Nonetheless the paper concluded that the treatment was useful in sportspeople and unlike many other studies used radiological measures of improvement.

A recent study taking place between Homerton University Hospital and Tottenham Hotspur Football Club found no significant difference between autologous blood injections and saline injections in the treatment of chronic patellar tendinopathy<sup>8</sup>. Both groups had statistically significant improvements in pain scores at 1 month after treatment, showing no advantage to the autologous blood injection treatment. This was a pilot study with a small number of patients enrolled (22).

A review article from 2015 looked at a number of trials involving platelet-rich plasma in the treatment of patellar tendinopathy<sup>9</sup>. There were limited studies included – 11 in total of which only 2 were randomised control trials. They concluded that platelet-rich plasma therapy appeared to be a safe and promising therapy which still lacks proven superiority over other treatments such as physical therapy.

Another review article from Korea looked at a large number of other studies, both RCTs and non-RCTs investigating use of platelet-rich plasma in patellar tendinopathy<sup>10</sup>. One of the RCTs studied compared platelet-rich plasma therapy to extracorporeal shockwave therapy (ESWT). This showed a significant improvement in the platelet-rich plasma group compared to the

ESWT group over a number of measures at both 6 and 12 month follow-up.

There has been some debate over whether it is the actual injection into the tendon or the local trauma caused by the needle which is of benefit to the healing process. A 2014 paper aimed to address this by comparing “dry needling” (insertion of the needle with no injection taking place) to platelet-rich plasma injection<sup>13</sup>. This study found that there was significantly more improvement in the platelet-rich plasma group at 12 weeks, but that over time this benefit dissipated and by 26 weeks there was no significant difference between the groups.

### **Use in ankle conditions**

A trial from a private sports medicine clinic aimed to compare standard treatment of Achilles tendinopathy (eccentric loading exercises) to standard treatment plus autologous whole blood injection<sup>14</sup>. They found a small short-term improvement with the addition of whole-blood injection to the treatment protocol but stated that double-blind RTCs would be necessary to draw more solid conclusions.

A Cochrane review looking at injection therapies broadly in Achilles tendinopathy<sup>15</sup> concluded that there is insufficient evidence to draw conclusions about the effectiveness of injection therapies in treatment of Achilles tendinopathy. They did not, however, look at different types of injection therapy individually and this review therefore combined both autologous whole blood and platelet-rich plasma with a number of other injections including corticosteroid, botulinum toxin and high-volume saline. As such this is of limited use in the assessment of platelet-rich plasma or autologous whole blood injections alone.

The majority of studies in this area use the VISA-A (Victoria Institute of Sport Assessment for Achilles Tendonopathy) which is a 8 question survey given to patients revolving around stiffness, pain during different activities and degree of sporting activity undertaken<sup>16</sup>. With this as the primary measure for most studies there is a lack of completely objective evidence around anatomical healing and recurrence rates.

### **Non-site specific studies**

A more generalised Cochrane review looked at the use of platelet-rich therapies in a variety of musculoskeletal soft tissue injuries including as an adjunct to recovery post-surgery<sup>11</sup>. The authors concluded that the evidence is of very low quality regarding all measures.

### **Whole blood versus platelet-rich plasma**

NICE guidance around autologous blood product injections for tendinopathy states that they found no substantial differences between platelet-rich plasma and whole blood injections<sup>1</sup>.

A double-blind randomised control study comparing injection of platelet-rich plasma to whole blood in the treatment of proximal hamstring tendinopathy<sup>12</sup> found that only the platelet-rich plasma group showed improvement from baseline at 6 months with regard to activities of daily living and IHOT-33 scores (International Hip Outcome Tool 33). However, the whole blood group showed statistically significant decreased pain on 15-minute sitting at 6 months. Ultrasound measures showed no difference between the groups.

As previously mentioned, a review piece looking at the use of platelet-rich plasma, whole blood and steroid injections in lateral epicondylitis found that platelet-rich plasma was significantly better at decreasing pain scores at 2 months, whilst whole blood provided significantly lower

measures of disability at 2 months and beyond compared to the other two treatments<sup>17</sup>.

### **Conclusions**

Given the variations in clinical results depending on which tendon is treated, it seems reasonable to assess the merits of the treatments based on the target location. When used to treat lateral epicondylitis, there does seem to be some evidence that in the long-term autologous blood injection does indeed lead to reduced pain (or duration of pain symptoms) compared to traditional corticosteroid treatment. None of the studies looked at here compared blood or platelet-rich plasma injection directly to more conservative measures such as physiotherapy. The release of the Cochrane review<sup>2</sup> will help to clarify whether there is any benefit of the treatment and where it could be found

When looking at the treatment of patellar tendinopathy the evidence is quite poor quality and conflicting. So far the reviews looking at this have generally concluded that there is insufficient evidence to support the use of autologous whole blood or platelet-rich plasma injections over traditional conservative therapies.

With regard to Achilles tendinopathy there is again a lack of sufficient evidence to conclude that there are any benefits to this treatment over more conservative management, and if there are any benefits then over what timescale they occur and which groups are most likely to benefit.

Given all of the above, it is not currently possible to say for certain if there is any benefit to these treatments, but they are generally concluded to be safe for use with minimal adverse events. As evidence for benefit is poor, we recommend against routinely funding these treatments until clear evidence of benefit is demonstrated.

### **References:**

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