Photoactivated platelet-rich plasma therapy for a traumatic knee chondral lesion

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SUMMARY

To evaluate the effect of combining photoactivation therapy with platelet-rich plasma injections in the treatment of a traumatic chondral lesion of the knee. A 38-year-old man presented with left-knee pain and swelling following a basketball injury. MRI demonstrated a full-thickness lateral tibial plateau chondral flap with subchondral cyst formation and marrow oedema. The patient underwent a course of photoactivated platelet-rich plasma (PAPRP) injections. Patient outcome measures included the numerical pain rating scale and the Western Ontario and McMaster Universities Arthritis Index 3.0 (WOMAC). Following treatment, the patient reported improvement in both pain and function as measured by the numerical pain-rating scale and WOMAC. MRI showed resolution of subchondral bone marrow bruising/oedema. No complications were noted. In this case report, PAPRP injections demonstrated improvement in all recorded outcome measures. Recognising the limitations of a single case report, the results highlight the need for more formal controlled trials to determine the potential use of PAPRP in the treatment of chondral lesions

BACKGROUND

The management of chondral injury/pathology presents a challenge to clinicians. The natural history of chondral defects is not well documented and although many studies indicate that they are progressive and lead to development of osteoarthritis,^{1 2} others are less conclusive.³ It is likely that progression is dependent upon variables such as patient's sex, age, weight, size and depth of lesion and also mechanism of injury.^{1 4} Current surgical management of traumatic and/or degenerative chondral lesions includes arthroscopic chondroplasty, microfracture/osteoplasty and when appropriate autologous chondrocyte implantation or matrix induced autologous chondrocyte implantation (MACI).

Regrettably, owing to the avascular nature of cartilage and subsequent lack of systemic regulation, cartilage regeneration has an inherently low healing potential.⁵ In the absence of bleeding, no fibrin clot or network is developed to act as a scaffold for tissue repair, and no inflammatory mediators or cytokines are released to stimulate cellular migration and proliferation. This leaves only the existing chondrocytes to facilitate the healing mechanism.

Given this, platelet-rich plasma (PRP) has been hypothesised as a promising cellular therapy for use in combination with autologous chondrocyte implantation.⁶ PRP preparation is a simple, low-cost and minimally invasive procedure that provides a natural concentrate of autologous

haemopoietically derived growth factors that can assist musculo-skeletal tissue repair. In vitro animal studies have demonstrated improved cartilage matrix expression with the use of PRP,⁷ whereas Marmotti *et al*⁸ have shown successful use of a PRP and chondrocyte scaffold in chondral defect repair beyond the use of a chondrocyte scaffold alone.

Furthermore, use of ultraviolet light activation (photoactivation) of peripheral blood has been shown to increase expression of leucocyte-derived anti-inflammatory mediators (interleukin 1 receptor antagonist) and also to cause reduction in proinflammatory cytokines (interleukin 2 and 6)^{9 10} that are thought to play a role in degenerative chondral pathology. Given that PRP alone has been shown to stimulate chondrocyte expression and have advantages with regard to pain relief,^{11–14} we postulate that a combined photoactivated platelet-rich plasma (PAPRP) preparation may offer a novel method for treatment of symptomatic chondral defects.

CASE PRESENTATION

Patient profile/summary

A healthy 38-year-old man presented to a Sports and Exercise Medicine Clinic complaining of left-knee pain, swelling, a sensation of 'catching' and episodes of instability, following a basketball injury 1 month back. Subsequent MRI showed a full-thickness lateral tibial plateau chondral flap with subchondral cyst formation and marrow oedema (figure 1A). He also had moderate partial thickness posterior lateral femoral condyle chondromalacia.

The site of the chondral flap correlated with the patient's area of persistent pain. Owing to the symptoms of catching and instability, he was advised to see an orthopaedic surgeon for arthroscopic assessment and likely chondroplasty.

Unfortunately, due to other unrelated family health issues, the patient was unable to undergo surgery and sought advice on alternative options. As the treating practitioner was involved in the use of PRP for osteoarthritis, PRP treatment was discussed. After supplying the patient with written information and education regarding photoactivated PRP, its use and the risks involved, the patient underwent a course of intra-articular PAPRP. Formal written consent was obtained prior to commencement of treatment.

INVESTIGATIONS

Imaging

MRI was performed prior to start of PAPRP treatment and again at week 15 (3 months postcompletion of the PAPRP course). Evaluation of the knee was performed using a 3-T MRI system (Verio;

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Figure 1 3-T MRI. (A) Initial MRI showing a full-thickness lateral tibial plateau chondral flap with subchondral cyst formation and marrow oedema. (B) MRI taken 3 months post-photoactivated platelet-rich plasma injections showing resolution of the subchondral bone marrow oedema but no structural change in the chondral flap.

Siemens Medical Solutions, Erlangen, Germany) with a dedicated eight-channel knee coil.

Proton density-weighted, fat-suppressed, fast spin-echo images, in the sagittal, coronal and axial planes, were acquired with the following pulse-sequence parameters: frequency bandwidth, 190 kHz; 3300/40 ms; section thickness, 3.0 mm; section gap, 0.3 mm; field of view, 15×15 cm; matrix size, 384×288; number of signals acquired, one; echo-train length, eight and flip angle 150°.

Proton density-weighted, fast spin-echo images, in the sagittal, coronal and axial planes, were acquired with the following pulse-sequence parameters: frequency bandwidth, 223 kHz; 3700/32 ms; section thickness, 3.0 mm; section gap, 0.3 mm; field of view, 15×15 cm; matrix size, 512×410; number of signals acquired, one; echo-train length, eight and flip angle 150°.

Treatment

The patient received a total of three PAPRP injections—each separated by 1 week (weeks 0, 1 and 2)

Photoactivated platelet-rich plasma preparation

Autologous blood (24 mls) was taken from the study participant and separated into 3×8.5 ml BD Vacutainers (BD, Franklin Lakes, NJ, USA) containing ACD (trisodium citrate, 22.0 g/l; citric acid, 8.0 g/l; and dextrose 24.5 g/l) to prevent clotting. The tubes were centrifuged at 1000 rpm for 10 min to create a platelet-poor plasma (PPP) level, a middle buffy coat level (high in platelets and leucocytes) and a red blood cell layer.

PPP was withdrawn from each tube to the level of 10 mm above the buffy coat and discarded. The remaining plasma, along with the buffy coat and 2 mm of the red cell layer were withdrawn into a single sterile tube and exposed to photoactivation for 10 min. Photoactivation was achieved using the commercial Adi-Light 2 device (AdiStem Ltd, Hong Kong).

Injection method

Under strict sterile conditions and ultrasound guidance, a sterile 21-gauge needle was inserted using an antero-lateral approach to the lateral knee compartment. Four millilitres of PAPRP were injected with no concurrent use of local anaesthetic.

Analysis method and outcome measures

Prospective analysis of patient outcomes to intra-articular PAPRP injection included the Numerical Pain Rating Scale (NPRS)¹⁵ and the validated Western Ontario and McMaster Universities Arthritis Index (WOMAC 3.0) for patients with knee osteoarthritis.^{16 17} The WOMAC Knee Score subsets cover pain, stiffness and physical function.

NPRS was recorded prior to all injections and on weeks 4, 7, 12 and 15. The WOMAC Knee Score was recorded prior to the first injection and at weeks 7, 12 and 15. In addition to the above treatment outcome measures, patient satisfaction was also assessed by recording a percentage-perceived improvement at week 15.

RESULTS

Pain scores were recorded on the NPRS preinjection and, then again, at intervals following PAPRP therapy. NPRS preinjection value of 3 improved to 0 at 7 weeks and remained 0 until the conclusion of data collection at week 15 (figure 2).

A similar trend was observed for the WOMAC Knee Score, where complete recovery was observed for all three WOMAC subsets between week 7 and 12 visits following treatment (figure 3). More importantly, the patient had functional improvement with resolution of his instability symptoms within 2 weeks of commencing treatment and noted a percentage-perceived improvement of 100% at week 15.

Figure 2 Numerical Pain Rating Scale. Pain reduced following photoactivated platelet-rich plasma injections for the treatment of a traumatic chondral defect in the knee.

Figure 3 Western Ontario and McMaster Universities Arthritis Index (WOMAC 3.0). Pain, stiffness and function improved following photoactivated platelet-rich plasma injections for the treatment of a traumatic chondral defect in the knee.

Repeat MRI performed at week 15 (3 months postcompletion of the PAPRP course) showed resolution of the subchondral bone marrow oedema although there was no change in the lateral tibial plateau chondral flap morphology or subchondral cyst (figure 1B).

No complications were noted during the course of PRP administration or during the monitored follow-up period.

DISCUSSION

PRP therapy has been proposed as a novel treatment modality for the management of articular cartilage injuries of the knee, a condition that is often plagued with healing difficulties. In this case study, we have combined photoactivation therapy with PRP in the hope of increasing the naturally derived anti-inflammatory mediators within PRP.

Following PAPRP therapy, the patient demonstrated improvement in all recorded treatment outcome measures. NPRS improved as early as week 1 (7 days post-first injection), suggesting an immediate analgesic benefit of PAPRP. By week 7, all three subsets of WOMAC had returned to asymptomatic levels, and remained improved until the final measurement at week 15 poststart of PAPRP treatment. Although this combined PAPRP preparation has not been reported in the literature for traumatic chondral lesions, intra-articular injections of PRP alone have been shown to similarly reduce pain and improve knee function in the treatment of knee osteoarthritis.¹⁸

PRP in sheep studies has been shown to improve cartilage repair after microfracture/osteoplasty when assessed at 6 months following therapy.¹⁹ Interestingly, in this case, despite the patient reporting functional improvement with resolution of mechanical symptoms of instability, the repeat MRI confirmed that tibial chondral pathology remained unchanged. In a study of 91 patients suffering from either degenerative chondropathy or osteoarthritis of the knee, and treated with PRP therapy, irrespective of the initial significant improvements in pain and function, by 24 months, cartilage degeneration was not seen to have improved.²⁰ As with the MRI follow-up in this case study, this suggests that PRP injections improved symptom control without affecting the tissue cartilage structure. This has significance if we accept that we need to improve the cartilage lesion so as to prevent development of progressive arthritis.

Of note, after surgical MACI, depending on the size of the lesion and grafted area, cartilage regeneration can often take up

to 12 months.²¹ Although no definite conclusions can be drawn from this single report, it can be postulated that chondrogenesis may take longer than the 15 weeks assessed here, or alternatively, PRP may cause only symptomatic improvement. Further long-term comparative studies will be required to determine whether combining PRP therapies with other modalities, such as photoactivation, may improve PRP's long-term outcomes and restorative capabilities.

Interestingly, repeat MRI at 15 weeks showed resolution of subchondral bone marrow bruising. Research indicates that the natural timecourse of traumatic bony bruising is inconsistent and resolution may occur within weeks or years.²² It has been suggested that the presence of persistent subchondral bone bruising on MRI may also be a marker for early degenerative arthritis.²² Furthermore, subchondral bone is heavily innervated and bony bruising is an accepted source of pain.²³ Although the patient's pain improved within 1 week of the initial PAPRP injection, the correlation of this with bone marrow bruising resolution is limited by the repeat MRI being performed at 15 weeks. Furthermore, in this limited single case report, whether PAPRP effectively influenced bony bruising resolution and hence pain relief is only a theoretical postulation.

CONCLUSION

Limited initial studies suggest that PRP may play a promising role in the active management of osteoarthritis and degenerative chondral lesions. To our knowledge, there is no published evidence of its use in acute and/or subacute chondral injuries and defects.

In this patient presenting with an acute traumatic chondral lesion, both pain and functionality testing indicate a positive outcome with photoactivated PRP therapy. Interestingly, the follow-up MRI showed complete clearance of subchondral bone marrow oedema though no change in the chondral lesion's morphology was noted. This may indicate that PRP plays a role in symptomatic management of chondral lesions/chondromalacia but may not encourage chondrogenesis. Alternatively, 15 weeks may be too early to observe chondral change on MRI imaging.

While recognising the low level of evidence and limitations of a single case report, the results described highlight the need to further investigate the use of PAPRP in the treatment of knee osteoarthritis and in degenerative and traumatic chondral lesion

conditions. Structured research in the form of appropriately powered controlled trials is needed to determine the symptom-modifying and structural disease-modifying properties of PAPRP.

Learning points

- In a single case report, platelet-rich plasma (PRP) has shown promise in treating symptomatic chondral injuries.
- Photoactivation therapy of PRP may improve its anti-inflammatory properties.
- Further research is required to determine if photoactivated platelet-rich plasma has structural disease modifying properties.

Competing interests None.

Patient consent Obtained.

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