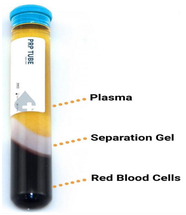

PLATELET-RICH PLASMA (PRP) INTRA-ARTICULAR INJECTION FOR OSTEOARTHRITIS OF THE KNEE - DOES IT AFFECT ARTICULAR CARTILAGE CONTENT? A SYSTEMATIC REVIEW AND META-ANALYSIS

Apostolos D. Prodromidis MD, MSc[1], Charalambos P Charalambous BSc, MBChB, MSc[2,3], Emma Moran MBChB[1], Ram Venkatesh FRCS(Orth)[1], Hemant Pandit MBBS, FRCS(Orth), DPhil(Oxon)[1,4]

Affiliations (UK): [1] Orthopaedic Department, Chapel Allerton Hospital, Leeds Teaching Hospitals NHS Trust, Leeds; [2] Orthopaedic Department, Blackpool Teaching Hospitals NHS Trust, Blackpool; [3] School of Medicine, University of Central Lancashire, Preston; [4] Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds.

ABSTRACT

INTRODUCTION / AIM: Platelet Rich Plasma (PRP) is increasingly used in the management of knee osteoarthritis. This study aimed to assess the effect of PRP on knee articular cartilage content (thickness and/or volume) and establish if there is a correlation between changes in cartilage and clinical outcomes in patients with knee osteoarthritis.

METHODOLOGY: A systematic review was performed following the Cochrane methodology in four online databases. Studies were included if they reported on cartilage content with MRI or Ultrasound before and after the injection. A random-effects model meta-analysis was performed. Correlation between the articular cartilage change and clinical outcomes was evaluated.

RESULTS: 14 studies (n=1,099) from 1,452 records met the inclusion criteria (Figure 1): seven RCTs (n=688), one prospective (n=50), one retrospective (n=68), and four case-series (n=224). The PRP treatment protocol varied widely. Follow-up ranged from 6-12 months. In meta-analysis, PRP treatment was not associated with a significant increase in cartilage thickness in either femoral condyle in isolation (Figures 2 and 3), or in the overall cartilage content (4 studies, n=187, standardized mean difference: Hedges g: 0.079; 95%CI: 0.358-0.516; p=0.723). Meta-analysis of 3 RCTs (n=112) showed no significant difference in the change of overall knee cartilage content with PRP injections compared with no PRP (Hedges 'g: 0.217; 95%CI: -0.177 – 0.611; P=0.281). There was no correlation between changes in cartilage and clinical outcomes following PRP treatment.

CONCLUSIONS: Treatment of knee osteoarthritis with PRP is not associated with a significant increase in articular cartilage content and any effect on cartilage post-PRP treatment is not associated with better clinical outcomes. A multi-centre, adequately powered RCT, with a standardised preparation/administration protocol assessing the long-term effect of PRP in knee osteoarthritis with high-resolution MRIs is needed to guide clinical care.

CONTACT

Apostolos D. Prodromidis
Orthopaedic Department, Chapel Allerton Hospital,
Leeds Teaching Hospitals NHS Trust, Leeds, UK
Email: prodromidisa@gmail.com

INTRODUCTION / AIM

Among the non-invasive treatment options for knee osteoarthritis (OA), intra-articular therapies are considered the mainstay of management. PRP has been increasingly used in recent years in the management of knee OA. Apart from improving symptoms and clinical outcomes, there is a suggestion that it may change the cartilage content possibly slowing or reversing OA. However, the level of evidence is low with some studies demonstrating no benefit.

The primary aim this study was to assess the effect of PRP on knee articular cartilage content (thickness and/or volume) in patients with symptomatic knee OA. The secondary aim was to establish if there is any correlation between changes in cartilage and clinical outcomes in patients with knee OA.

METHODS

A systematic review was performed following the Cochrane methodology for systematic reviews in four online databases (MEDLINE, EMBASE, CINAHL, CENTRAL).

Inclusion/exclusion criteria:
Study designs: RCTs, prospective and retrospective cohort studies, case-control studies and case series with minimum 3-month follow-up.
Population: Adults with knee OA.
Intervention/Comparators: Adults with knee OA having treatment with intraarticular injection with PRP. Studies were included if they reported on cartilage content with Ultrasound or MRI before and after the injection.
Outcomes: Articular cartilage content (thickness and/or volume) measured and/or mapped using cross-sectional imaging (Ultrasound or MRI).

Data analysis/Statistical analysis
For each study, cartilage thickness/volume or cartilage mapping values on MRI or Ultrasound were reported in absolute numbers and rates and any significant difference post-injection was established (p<0.05). For studies reporting on cartilage thickness, pre- and post-injection differences in means and 95% CIs were calculated and combined in a random-effects model meta-analysis.
Correlation between the articular cartilage change and clinical outcomes was evaluated.

RESULTS

14 studies (n=1,099) from 1,452 records met the inclusion criteria (Figure 1): seven RCTs (n=688), one prospective (n=50), one retrospective (n=68), and four case-series (n=224). The total number of participants included was 1,099 (1,169 TKAs).

Where a control group was available the comparison was made with: hyaluronic acid or a placebo or conservative management with an exercise program.

Age range was 18-88 years. The mean BMI in all the studies was less than 30kg/m^2. The PRP treatment protocol varied widely. Follow-up ranged from 6-12 months.

Nine studies used MRI and five studies high-resolution ultrasound to evaluate cartilage thickness or volume.
Among the nine studies that used MRI to evaluate cartilage thickness, three reported significant improvement post-PRP injections.
Among the five studies that used ultrasound to evaluate cartilage thickness, one case series (n=103) reported significant improvement in cartilage thickness on the MFC six months following three PRP injections.

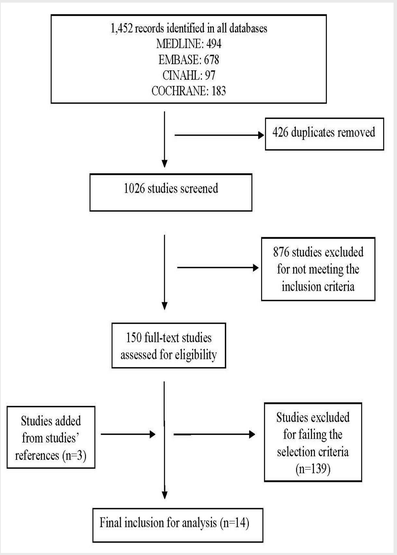

Figure 1. Methodology of identification and selection of studies (PRISMA flow chart)

RESULTS

Five studies (n=313) measured the cartilage thickness in MFC pre- and post-PRP treatment. Meta-analysis did not show a significant increase in cartilage thickness post-PRP treatment (Figure 2: estimated difference in means: 0.068; 95%CI: -0.050 - 0.185; p=0.259).

Four studies (n=210) measured the cartilage thickness in LFC. Meta-analysis did not show a significant increase in cartilage thickness post-PRP treatment (Figure 3: estimated difference in means: 0.064; 95%CI: -0.02 – 0.148; P=0.136).

Three RCTs (n=112) compared PRP treatment with a control. One (n=40) compared PRP with HA [26], whilst the other two compared PRP with exercise program.

Meta-analysis showed no significant difference in cartilage thickness and/or volume with PRP (Hedges 'g: 0.217; 95%CI: -0.177 – 0.611; P=0.281; heterogeneity: τ^2=0.039; I^2=31.548; Q=2.922; P=0.232).
Thirteen studies reported on various clinical outcomes such as WOMAC, KOOS, IKDC, VAS, SF-36, Lysholm and Tegner score. Clinical outcomes significantly improved in all studies irrespective of the effect on cartilage.

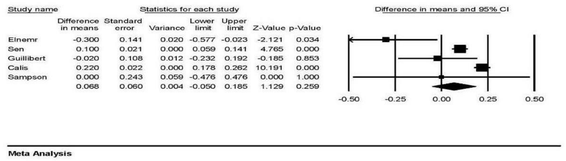

Figure 2. Forest plot for the estimated differences in mean cartilage thickness of medial femoral condyle post-PRP treatment.

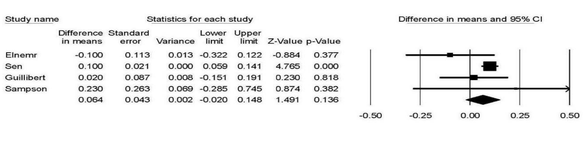

Figure 3. Forest plot for the estimated differences in mean cartilage thickness of lateral femoral condyle post-PRP treatment.

CONCLUSIONS

Analysis of the current literature shows that treatment of knee OA with PRP is not associated with a significant increase in articular cartilage content and any effect on cartilage post-PRP treatment that may exist is not associated with better clinical outcomes.

A multi-centre, adequately powered RCT, with a standardised preparation/administration protocol assessing the long-term effect of PRP in knee OA with high-resolution MRIs is needed to provide definitive guidance to clinical care both for managing OA and for its use in cartilage regeneration.

Until such high-quality evidence becomes available, we recommend that PRP is not administered with the intention of promoting chondrogenesis.

REFERENCES

1. Raeissadat SA, Ghorbani E, Sanei Taheri M, et al. MRI Changes After Platelet Rich Plasma Injection in Knee Osteoarthritis (Randomized Clinical Trial). J Pain Res. 2020;13:65-73.
2. Bennell KL, Paterson KL, Metcalf BR, et al. Effect of Intra-articular Platelet-Rich Plasma vs Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients With Knee Osteoarthritis: The RESTORE Randomized Clinical Trial. Jama. 2021 Nov 23;326(20):2021-30.
3. Bansal H, Leon J, Pont JL, et al. Platelet-rich plasma (PRP) in osteoarthritis (OA) knee: Correct dose critical for long term clinical efficacy. Sci Rep. 2021 Feb 17;11(1):3971.
4. Calis HT, Sütbeyaz ST, Güler E, et al. Efficacy of intra-articular autologous platelet rich plasma application in knee osteoarthritis. Turkish Journal of Rheumatology. 2015;30(3):198.
5. Cobianchi Bellisari F, De Marino L, Arrigoni F, et al. T2-mapping MRI evaluation of patellofemoral cartilage in patients submitted to intra-articular platelet-rich plasma (PRP) injections. La radiologia medica. 2021 2021/08/01;126(8):1085-94.
6. Elnemr RA, Abdelnaby HM, Elshafei MM. Does Intra-Articular Platelet Rich Plasma Injection Improve Meniscal Repair Outcomes? Asian J Sports Med. 2019;10(3):e85360.#
7. Guillibert C, Charpin C, Raffray M, et al. Single Injection of High Volume of Autologous Pure PRP Provides a Significant Improvement in Knee Osteoarthritis: A Prospective Routine Care Study. Int J Mol Sci. 2019 Mar 15;20(6).
8. Hart R, Safi A, Komzák M, et al. Platelet-rich plasma in patients with tibiofemoral cartilage degeneration. Arch Orthop Trauma Surg. 2013 Sep;133(9):1295-301.
9. Kenmochi M. Clinical outcomes following injections of leukocyte-rich platelet-rich plasma in osteoarthritis patients. J Orthop. 2020 Mar-Apr;18:143-9
10. Hart R, Safi A, Jajtner P, et al. Tibiofemoral chondromalacia treated with platelet-rich plasma and hyaluronic acid. Current Orthopaedic Practice. 2017;28(1):58-65.
11. Sampson S, Reed M, Silvers H, et al. Injection of platelet-rich plasma in patients with primary and secondary knee osteoarthritis: a pilot study. Am J Phys Med Rehabil. 2010 Dec;89(12):961-9.
12. Şen E, Yıldırım MA, Yeşilyurt T, et al. Effects of platelet-rich plasma on the clinical outcomes and cartilage thickness in patients with knee osteoarthritis. J Back Musculoskelet Rehabil. 2020;33(4):597-605.
13. Buendía-López D, Medina-Quirós M, Fernández-Villacañas Marín M. Clinical and radiographic comparison of a single LP-PRP injection, a single hyaluronic acid injection and daily NSAID administration with a 52-week follow-up: a randomized controlled trial. J Orthop Traumatol. 2018 Aug 20;19(1):3.
14. Elik H, Doğu B, Yılmaz F, et al.. The efficiency of platelet-rich plasma treatment in patients with knee osteoarthritis. J Back Musculoskelet Rehabil. 2020;33(1):127-38.