

Photo-Activated Platelet Rich Plasma Injection for Knee Osteoarthritis: Two-Year Experience with 32 Cases

Tangtong N, MD¹, Chaiyapat M, BS¹, Ratanachai W, MD¹, Pongpirul K, MD, MPH, PhD^{2,3,4}

¹ Department of Orthopedics, Bumrungrad International Hospital, Bangkok, Thailand

² Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

³ Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

⁴ Bumrungrad Research Center, Bumrungrad International Hospital, Bangkok, Thailand

Background: While severe knee osteoarthritis (OA) requires surgery, most patients suffering mild OA symptoms need only medical management. Evidence of intra-articular injection with autologous photo-activated platelet-rich plasma (PA-PRP) has been limited to the findings from a pilot study in a controlled setting with a small sample size. The authors reported a 2-year experience with the use of PA-PRP in patients with OA of the knee.

Objective: To report the clinical outcomes of PA-PRP injection in treatment of OA of the knee.

Materials and Methods: Demographic and clinical data of all patients with knee OA that received PA-PRP injection at Bumrungrad International Hospital between May 2014 and May 2016 were analyzed. Clinical outcome was assessed at baseline before the first, second, and third dose, and 1, 3, 6, 9, 12, 18, 24 months after the PA-PRP injection using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

Results: Thirty-two patients received PA-PRP during the study period. Forty percent of these patients had OA of both knees. Baseline WOMAC score of 39.2 on average was reduced by one-third after the first dose of PA-PRP. Three months after the full course of three doses, WOMAC score was improved by 80% from baseline. Six patients (5.3%) got worse WOMAC scores after their first dose of PA-PRP, but insisted on completing the course and eventually saw clinical improvement.

Conclusion: Clinical benefits of PA-PRP injection could last for approximately three months after a full course of injection. Worse WOMAC score after the first injection might occur in 5% of the patients.

Keywords: Knee osteoarthritis, Platelet rich plasma

J Med Assoc Thai 2019;102(6): 720-3

Website: <http://www.jmatonline.com>

Received 3 May 2017 | Revised 1 Sep 2017 | Accepted 4 Sep 2017

Osteoarthritis (OA) of the knee has been prevalent globally. It is estimated that at least 10% of the worldwide population aged older than 60 years may have symptoms of this condition⁽¹⁾. Mortality and morbidity significantly impact the economic cost⁽²⁾, which will be worsened by extended life expectancy⁽³⁾.

While severe knee OA requires surgery, the current therapeutic approaches focus on symptomatic medical

management with Non-steroidal Anti-Inflammatory Drugs (NSAIDs)⁽⁴⁾ as well as delaying the structural and functional changes of milder OA⁽⁵⁾. Intra-articular injection with corticosteroids, hyaluronic acid (HA), growth factor, and needle lavage has been used with limited supporting evidence⁽⁴⁾.

Given potential tissue regeneration from reduced inflammation by growth factors and other cytokines released by platelets in response to injury⁽⁶⁾, autologous platelet-rich plasma (PRP) has been proposed as an alternative treatment for OA of the knee⁽⁷⁾ and proven to be safe and efficacious⁽⁸⁾. The platelet-produced substances form a matrix that promotes migration of additional cells to the area, resulting in improved tissue healing and alleviating the inflammation of OA^(6,9). PRP was shown to be superior short-term (24 and 48

Correspondence to:

Pongpirul K.

Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, 1873 Rama IV Road, Patumwan, Bangkok 10330, Thailand.

Phone: +66-86-6055088

Email: doctorkrit@gmail.com

How to cite this article: Tangtong N, Chaiyapat M, Ratanachai W, Pongpirul K. Photo-Activated Platelet Rich Plasma Injection for Knee Osteoarthritis: Two-Year Experience with 32 Cases. J Med Assoc Thai 2019;102:720-3.

weeks) for pain, stiffness, and functional improvement compared to HA in a randomized controlled trial in alleviating symptoms of mild to moderate OA of the knee^(10,11).

To improve clinical outcomes, photo activation was applied in the PRP preparation (PA-PRP). Experiences with one injury⁽¹²⁾ and two OA cases^(13,14) with satisfactory clinical outcomes from PA-PRP were reported. The effectiveness of PA-PRP in knee OA was later compared with hyaluronic acid in a recent randomized controlled pilot study, which reported better feasibility, safety, short-term symptomatic, and functional changes⁽¹⁵⁾. The present study was aimed to report our 2-year experience with the use of PA-PRP in patients with OA of the knee.

Materials and Methods

Demographic and clinical data of all patients with knee OA received PA-PRP injection at Bumrungrad International Hospital between May 2014 and May 2016 were analyzed. Patients who were not improved by conventional medical treatment or refused surgical option were eligible for PA-PRP. Clinical outcome was assessed at baseline before the first, second, and third dose, and 1, 3, 6, 9, 12, 18, 24 months after PA-PRP injection using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

The PA-PRP was done using AdiStem (Adistem Ltd., Australia). During the procedure, 32 mL of sterile blood was drawn. The syringe was placed in the centrifugal machine and spun at 200 g for 10 minutes. PRP was obtained by removing the plasma component that contains more platelets. The collected PRP tube was placed under Adistem Adilight-2 for 10 minutes to photo-activate. The first dose of PA-PRP was injected into the affected knee, followed by the second and third doses around two and four weeks, respectively.

Descriptive statistics were used where appropriate. The improvement of WOMAC scores at each visit was assessed by comparing with the first visit, using Student's t-test.

Ethics approval

The present study was approved by the Bumrungrad International Institutional Review Board (BI-IRB No.224-03-16).

Results

Thirty-two patients received PA-PRP during the study period. They were middle-aged Thai or Mongolian female (Table 1). Forty percent of the patients had OA of both knees.

Table 1. Patients' characteristics (n=32)

Characteristics	n (%)
Age (years), Mean±SD	57.8±12.4
Female	19 (59.4)
Nationality	
Thai	11 (34.4)
Mongolian	18 (56.3)
German	1 (3.1)
Indian	1 (3.1)
Myanmar	1 (3.1)
Affected side of knee	
Right	11 (34.4)
Left	8 (25.0)
Both	13 (40.6)

SD=standard deviation

Table 2. Average WOMAC Score at different time points

Time points	WOMAC score Mean±SD	p-value
Before 1 st injection (baseline)	39.2±15.4	(reference)
Before 2 nd injection	26.3±15.5	0.002
Before 3 rd injection	20.8±16.2	<0.001
3-month follow-up	8.1±6.2	<0.001
6-month follow-up	18.6±13.7	<0.001
9-month follow-up	26±18.3	0.016
12-month follow-up	26.8±19.3	0.043
18-month follow-up	6±8.5	0.005
24-month follow-up	17.3 ± 28.3	0.009

WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index; SD=standard deviation

Baseline WOMAC score of 39.2 on average was reduced by one-third after the first dose of PA-PRP (Table 2). Additional 23 percent improvement was achieved after the second dose (p=0.002). Three months after the full course of three doses, WOMAC score was improved by 80% from baseline (p<0.001). However, the clinical outcome seemed to diminish afterward but still better than the baseline.

Six patients (5.3%) had worse WOMAC scores after their first dose of PA-PRP but insisted on continuing with the second and third doses. Five had eventual WOMAC score improvement, whereas one (patient No.25) reported better pain without WOMAC

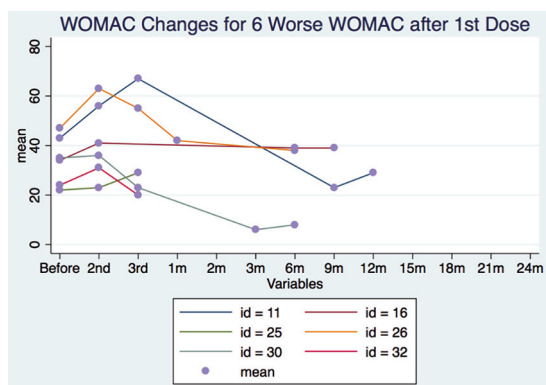


Figure 1. WOMAC changes in 6 patients who had worse score after 1st dose of PA-PRP.

score assessment (Figure 1).

Discussion

The present study confirmed the clinical benefit of PA-PRP as suggested in the previous randomized controlled pilot study⁽¹⁵⁾ in a real-life setting with no serious adverse event. In that study, 11 and 10 received PA-PRP and HA after randomization, respectively. Despite a well-controlled setting, small sample size and short follow-up period limited the clinical application of PA-PRP in the actual practice. The present study not only reported clinical outcomes at longer term in a larger group of patients, but also reported two practical lessons.

The authors added that worsen WOMAC score after the first injection was common (approximately 5%) and the actual clinical outcome should be assessed after the full course was given. In addition, the improvement of WOMAC score sustained for approximately three months after a full course of PA-PRP injection. It could be implied that additional injection of PA-PRP might be needed. Nonetheless, the authors were unable to conclude whether a full course or a single injection of PA-PRP should be repeated. This question warrants further study.

Conclusion

Clinical benefits of PA-PRP injection could last for approximately three months after full course of injection. Worse WOMAC score after the first injection might occur in 5% of the patients.

What is already known on this topic?

The PA-PRP, when injected into a knee OA, will improve both pain and function for the patient. However, it is a clinical procedure with temporary

improvement. The results of the injection are not permanent and depend on the severity of the knee arthritic.

What this study adds?

This study emphasizes the effects of PA-PRP in terms of a longitudinal aspect of two years. The overall results also indicate that the decrease in WOMAC scores after the first injection is common and patients are advised to continue until full course is completed for improved and satisfied results.

Acknowledgement

The authors would like to thank Miss Atthawon Chotisean for assistance in development of the present research. She had supported us in term of counseling and communication amongst different parties. This research would not have been smoothly accomplished without her.

Authors' contributions

Tangtong N, Ratanachai W, and Pongpirul K conceptualized and initiated the study. Tangtong N and Chaiyapat M collected and verified the data. Chaiyapat M and Pongpirul K analyzed the data. Tangtong N, Chaiyapat M, and Pongpirul K drafted the manuscript. All authors read and approved the final version of the manuscript.

Potential conflicts of interest

The authors declare no conflict of interest.

References

- Pereira D, Peleteiro B, Araujo J, Branco J, Santos RA, Ramos E. The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review. *Osteoarthritis Cartilage* 2011;19:1270-85.
- Wielage RC, Myers JA, Klein RW, Happich M. Cost-effectiveness analyses of osteoarthritis oral therapies: a systematic review. *Appl Health Econ Health Policy* 2013;11:593-618.
- Hilgsmann M, Cooper C, Arden N, Boers M, Branco JC, Luisa BM, et al. Health economics in the field of osteoarthritis: an expert's consensus paper from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). *Semin Arthritis Rheum* 2013;43:303-13.
- American Academy of Orthopaedic Surgeons (AAOS). Treatment of osteoarthritis of the knee evidence-based guideline. 2nd ed. Rosemont, IL: AAOS; 2013.
- Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis, part I: critical appraisal of existing treatment guidelines

- and systematic review of current research evidence. *Osteoarthritis Cartilage* 2007;15:981-1000.
6. Andia I, Maffulli N. Platelet-rich plasma for managing pain and inflammation in osteoarthritis. *Nat Rev Rheumatol* 2013;9:721-30.
 7. Spakova T, Rosocha J, Lacko M, Harvanova D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. *Am J Phys Med Rehabil* 2012; 91:411-7.
 8. Anitua E, Sanchez M, Aguirre JJ, Prado R, Padilla S, Orive G. Efficacy and safety of plasma rich in growth factors intra-articular infiltrations in the treatment of knee osteoarthritis. *Arthroscopy* 2014;30:1006-17.
 9. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med* 2009;37:2259-72.
 10. Sanchez M, Fiz N, Azofra J, Usabiaga J, Aduriz RE, Garcia GA, et al. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. *Arthroscopy* 2012;28:1070-8.
 11. Vaquerizo V, Plasencia MA, Arribas I, Seijas R, Padilla S, Orive G, et al. Comparison of intra-articular injections of plasma rich in growth factors (PRGF-Endoret) versus Durolane hyaluronic acid in the treatment of patients with symptomatic osteoarthritis: a randomized controlled trial. *Arthroscopy* 2013;29:1635-43.
 12. Freitag J, Barnard A, Rotstein A. Photoactivated platelet-rich plasma therapy for a traumatic knee chondral lesion. *BMJ Case Rep* 2012;2012. pii:bcr2012006858.
 13. Freitag J, Barnard A. The next step in osteoarthritis management—Photoactivated Platelet Rich Plasma injections: A case study. *J Sci Med Sport* 2012;15 Suppl 1:S136.
 14. Freitag JB, Barnard A. To evaluate the effect of combining photo-activation therapy with platelet-rich plasma injections for the novel treatment of osteoarthritis. *BMJ Case Rep* 2013;2013. pii:bcr2012007463.
 15. Paterson KL, Nicholls M, Bennell KL, Bates D. Intra-articular injection of photo-activated platelet-rich plasma in patients with knee osteoarthritis: a double-blind, randomized controlled pilot study. *BMC Musculoskelet Disord* 2016;17:67.