Original Article

Role of Platelet Rich Plasma in Osteoarthritis of the Knee Joint

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Abstract

Background: Osteoarthritis (OA) is a leading cause of disability and doubles the number of visits to primary care practitioners for those with the condition in comparison to those without. OA affects the knee more often than any other joint, Platelet-rich plasma (PRP) is a concentrate of autologous blood growth factors which has been shown to provide some symptomatic relief in early osteoarthritis (OA) of the knee. **Objective:** the aim of this prospective study is to demonstrate the effectiveness of prp injection in patients with OA of the knee. **Materials and Methods:** 60 patients with 74 knees affected by variable grades of OA were enrolled in our study in Alwasity teaching hospital from January 2018 to December 2019 with follow up till December 2021. 49 patients with 62 knees were females and 11 patients with 12 knees were males, all patients received three injections of prp at weekly intervals and were followed up every three months for two years. **Results:** After one year of follow up 11 knees with KL-G I had decrease in VAS score to 0–2 (73.3%),19 knees with KL-G II had decrease of VAS score to 1–3 (70.3%),10 knees with KL-G III had decrease of VAS score to 4–5 (40%), All 7 knees with KL-G IV didn't have any response during treatment or at the end of 1st year. All patients had scores similar to that before starting treatment at the end of 2nd year. **Conclusion:** The present state of knowledge holds promise for PRP of certain specifications for pain management in early OA knee. PRP has consistently been shown by various clinical studies to be useful in OA of the knee. Nevertheless, a lot of grey areas remain in our understanding of PRP and OA, and many more focused clinical and *in vitro* studies are required. PRP seems to be an evolving future trend.

Keywords: Knee joint, osteoarthritis, platelet rich plasma, role

Introduction

Although osteoarthritis (OA) is one of the most prevalent musculoskeletal diseases in the world, its treatment is still relatively limited.[1] There is little evidence that the currently used drugs have effective action against the progression of the disease. A relatively new strategy for the treatment of OA is the use of cell elements and biomediators of tissue response. In this context, the platelet-rich plasma (PRP) has been configured as a perspective for improving clinical and structural outcomes by delivering a high concentration of growth factors that mediate cartilage healing and remodeling. Its potential has been shown *in vitro* and *in vivo* studies, however its real efficacy in OA is not well established.[2,3] **Mechanism of action of PRP:** Growth factor affect(Platelet-derived growth factor (PDGF)) angiogenesis; macrophage activation; proliferation and chemotaxis of fibroblasts; collagen synthesis and enhanced proliferation of bone cells by Transforming growth factor-β (TGF-β),fibroblasts proliferation; synthesis of type I collagen and fibronectin; deposition of bone matrix; inhibition of bone resorption by Platelet-derived epidermal growth factor (PDGF); Vascular endothelial growth factor (VEGF) lead to vascularisation; stimulation of vascular endothelial cells by Insulin-like growth factor 1 (IGF-I), fibroblasts chemotaxis; protein synthesis stimulation; enhanced bone formation by Platelet factor 4 (PF4), Enhanced influx of neutrophils; chemoattractant for fibroblasts by epidermal growth factor (EGF), cellular proliferation and differentiation by hepatocyte growth factor (HGF), Inhibition of NF-κB transactivation activity; anti-inflammatory action through inhibition of monocyte-like chemotaxis by Stromal-cell-derived growth factor-1α (SDF-1α) Supports primary adhesion and migration of progenitor cell.[4,5] Plasma PRP is obtained by

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Website: www.medjbabylon.org

DOI: 10.4103/MJBL.MJBL_9_22

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Submission: 12-Jan-2022 **Accepted:** 15-Feb-2022 **Published:** 29-Sep-2022

How to cite this article: Redah SM. Role of platelet rich plasma in osteoarthritis of the knee joint. Med J Babylon 2022;19:354-7.

centrifuging the autologous venous blood, causing a high concentration of platelets in a small volume of plasma. There is no standardization regarding the speed, duration and number of centrifugations needed, neither which layer exactly is removed from the precipitate after this process.[6] Single vs double centrifugation technique. PPP vs PRP. With or without WBC. Activated vs non activated platelets.[6] Recently some authors developed a classification of the different types of PRP, according to the platelet count, the activator used, and the presence of white blood cells. This system was called PAW (Platelets, Activation and White Blood Cells).The classification, however, is complex and its practical significance has not been established yet.[7,8] Local symptoms are the most common adverse events, ranging from pain at the injection site to signs of arthritis. The way of obtainment of PRP influences the degree of intra-articular inflammatory response, with this effect being attributed to the number of leukocytes present in the infiltrate. Allergic reactions are possible but rare effects since it is an autologous product. The most feared complication is the intra-articular infection that can be prevented by performing the aseptic procedure. The most frequently reported adverse events were arthralgia in the injected joint, whose intensity varied from mild to moderate, and its resolution occurred in days, extending to weeks in the most severe cases. Case of hypertrophy of the regenerated cartilage tissue diagnosed by an arthroscopy performed because of the patient's symptoms, and was resolved by local debridement. Case of rash after the injection, the resolution of which was spontaneous, with no need for specific treatment. Higher post-injection pain was noted in those patients injected with PRP compared to HA. Systemic symptoms and infections were not reported in the analyzed studies.[9,10] The aim of this prospective study is to demonstrate the effectiveness of prp injection in patients with mild to moderate OA of the knee.

Materials and Methods

60 patients with 74 knees affected by variable grades of OA were enrolled in a prospective study in Al-wasity teaching hospital from January 2018 to December 2019 with follow up till December 2021 .49 patients with 62 knees were females and 11 patients with 12 knees were males. ages ranging from 35 to 70,only patients with primary OA with no history of previous trauma, inflammatory arthritis or intraarticular injections were included in this study.

We used three criteria in assessment of patients:

1. the severity of pain assessed by VAS grading (visual analogue scale)
2. the severity of OA of the knee assessed by Kellgren Lawrence grading
3. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Table 1: Illustration of number of patients and their sccores

Kellegren lawrance grading	Number of knees	Vas score	WOMAC index
I	15	2–5	10–24
II	27	3–6	26–50
III	25	5–8	53–72
IV	7	6–9	75–90

15 knees were KL grade I with VAS grading ranging from 2 to 5 with WOMAC index from 10 to 24

27 knees were KL grade II with VAS grading ranging from 3 to 6 with WOMAC index from 26 to 50

25 knees were KL grade III with VAS grading ranging from 5 to 8 with WOMAC index from 53 to 72

7 knees were KL grade IV with VAS grading ranging from 6 to 9 with WOMAC index from 75 to 90 as illustrated in Table 1.

We collected 40 cc of blood from the patient in vacuum citrated tubes

We used double centrifugation method at 2000 rpm, 10 minutes each

After the second centrifugation we collected the platelet precipitate of each tube under conventional sterile environment (using benzene light) finally getting about 4 cc of PRP.

We didn't activate the platelet

The PRP was injected under sterile technique in the affected knee using the retro-patellar injection method.

Each patient received three injections at weekly intervals

We scored the VAS score, the Kellgren Lawrence grading and the WOMAC index for each patient at presentation and every three months for 2 years.

Our radiographic standardization for the knees was 75 cm of the tube from the patient with x-ray beam directed at the lower pole of the patella for the weight bearing x-ray.

All patients received NSAID and other types of analgesia for one week only after starting treatment to minimize interference with the response to injections.

We didn't encounter any major complications after injection of PRP other than mild irritation at the site of injection which was controlled by NSAID.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form

Table 2: Response of patients with KL-G-I

Response	Number of knees	VAS sore before PRP	VAS score after 1 year of PRP	WOMAC index before PRP	WOMAC index after 1 year of PRP
Knees with response	11	2–5	0–2	10–24	5–9
Knees with no response	4	2–5	2–5	10–24	10–24

Table 3: Response of patients with KL-G-II

Response	Number of knees	VAS sore before PRP	VAS score after 1 year of PRP	WOMAC index before PRP	WOMAC index after 1 year of PRP
knees with response	19	3–6	1–3	26–50	11–15
knees with no response	8	3–6	3–6	26–50	26–50

Table 4: Response of patients with KL-G-III

Response	Number of knees	VAS sore before PRP	VAS score after 1 year of PRP	WOMAC index before PRP	WOMAC index after 1 year of PRP
knees with response	10	5–8	4–5	53–72	16–19
knees with no response	15	5–8	5–8	53–72	53–72

were reviewed and approved by a local ethics committee according to the document number 78 (including the number and the date in 4/11/2017) to get this approval.

Results

After one year of follow up 11 knees with KL-G I had decrease in VAS score to 0–2 and WOMAC index 5 to 9 (73.3%) [Table 2].

19 knees with KL-G II had decrease of VAS score to 1–3 and WOMAC index 11 to 15 (70.3%) [Table 3].

10 knees with KL-G III had decrease of VAS score to 4–5 and WOMAC index 16 to 19 (40%) [Table 4].

All 7 knees with KL-G IV didn't have any response during treatment or at the end of 1st year.

All KL-G I-III had gradual deterioration of response during the 2nd year, all of them had VAS scores and WOMAC index similar to that before the onset of treatment at the end of the 2nd year.

There was no improvement in radiographic grading during or after the end of treatment in all patients.

We noticed mild improvement in the range of motion of the knee specially in KL-G I and II.

Discussion

All patients completed the intervention and all outcome measures. There were no losses to follow-up, most of patients with KL-G I-III had significant improvement in their pain scores and functional performance as guided by WOMAC index, the only functional modality that didn't have significant improvement with treatment is stiffness. This therapy appears to be associated with significant improvements in pain, patient satisfaction and goal-orientated outcomes.[11,12] Pilot and prospective studies investigating the clinical efficacy of intra-articular injections of PRP in patients with knee OA have demonstrated clinical improvement in self-reported pain and functional capacity with no major adverse effects.[13,14] In a recent related systematic review, conducted by Pilot et.al. team included six randomised controlled trials comparing the effectiveness of PRP to other intra-articular injections, exercise or analgesia for a minimum of 6 months. PRP injections were found to produce statistically significant improvements in overall WOMAC scores for patients with knee osteoarthritis up to 12 months after intervention.[15,16] The risk of adverse events in PRP-treated participants was not significantly increased in comparison with other knee osteoarthritis treatment options[17] These findings are consistent with much recently published research involving PRP as an intervention in knee OA.[11,12]

Conclusion

This study has demonstrated that it is feasible and safe to deliver PRP therapy in primary care for knee osteoarthritis. The present state of knowledge holds promise for PRP of certain specifications for pain management in early OA knee. PRP has consistently been shown by various clinical studies to be useful in OA of the knee. Nevertheless, a lot of grey areas remain in our understanding of PRP and OA, and many more focused clinical and *in vitro* studies are required. PRP seems to be an evolving future trend. Researchers are also focused on developing a better PRP product by combining it with various molecules such as

gelatin, chitosan and others. PRP is definitely there to stay for OA therapy use in future.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Wright EA, Katz JN, Cisternas MG, Kessler CL, Wagenseller A, Losina E. Impact of knee osteoarthritis on health care resource utilization in a US population-based national sample. Med Care 2010;48:785-91.
2. Duymus TM, Mutlu S, Dernek B, Komur B, Aydogmus S, Kesiktas FN. Choice of intra-articular injection in treatment of knee osteoarthritis: Platelet-rich plasma, hyaluronic acid or ozone options. Knee Surg Sports Traumatol Arthrosc 2017;25:485-92.
3. Patel S, Dhillon MS, Aggarwal S, Marwaha N, Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: A prospective, double-blind, randomized trial. Am J Sports Med 2013;41:356-64.
4. Lee KS, editor. Platelet-rich plasma injection. In: Seminars in Musculoskeletal Radiology. New York: Thieme Medical Publishers; 2013.
5. Lana JF, Weglein A, Sampson SE, Vicente EF, Huber SC, Souza CV, *et al*. Randomized controlled trial comparing hyaluronic acid, platelet-rich plasma and the combination of both in the treatment of mild and moderate osteoarthritis of the knee. J Stem Cells Regen Med 2016;12:69-78.
6. Spaková T, Rosocha J, Lacko M, Harvanová 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.
7. Say F, Gürler D, Yener K, Bülbül M, Malkoc M. Platelet-rich plasma injection is more effective than hyaluronic acid in the treatment of knee osteoarthritis. Acta Chir Orthop Traumatol Cech 2013;80:278-83.
8. Reuben DB, Tinetti ME. Goal-oriented patient care–an alternative health outcomes paradigm. N Engl J Med 2012;366:777-9.
9. Billingham SA, Whitehead AL, Julious SA. An audit of sample sizes for pilot and feasibility trials being undertaken in the united kingdom registered in the united kingdom clinical research network database. BMC Med Res Methodol 2013;13:104.
10. Szende A, Oppe M, Devlin N, editors. EQ-5D Value Sets: Inventory, Comparative Review and User Guide. New York: Springer Science &Business Media; 2007.
11. 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.
12. Mustafa A, Mallen CDM, Murphy AWM, Glynn LG, editors. The Effectiveness and Safety of Platelet-Rich Plasma Intra-Articular Injections in the Treatment of Knee Osteoarthritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Limerick: Health Research Institute Annual Scientific Meeting; 2017.
13. Shen L, Yuan T, Chen S, Xie X, Zhang C. The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: Systematic review and meta-analysis of randomized controlled trials. J Orthop Surg Res 2017;12:16.
14. Cerza F, Carnì S, Carcangiu A, Di Vavo I, Schiavilla V, Pecora A, *et al*. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. Am J Sports Med 2012;40:2822-7.
15. Simental-Mendía M, Vílchez-Cavazos JF, Peña-Martínez VM, Said-Fernández S, Lara-Arias J, Martínez-Rodríguez HG. Leukocyte-poor platelet-rich plasma is more effective than the conventional therapy with acetaminophen for the treatment of early knee osteoarthritis. Arch Orthop Trauma Surg 2016;136:1723-32.
16. DeLong JM, Russell RP, Mazzocca AD. Platelet-rich plasma: The PAW classification system. Arthroscopy 2012;28:998-1009.
17. Jang SJ, Kim JD, Cha SS. Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. Eur J Orthop Surg Traumatol 2013;23:573–80.