Unified Journals

2015-2250

Unified Journal of Medicine and Medical Sciences
Vol 1(1) pp. 001- 005 August, 2015.
http://www.unifiedjournals.org/ujmms

Full Length Research Paper

Is Platelet-Rich Plasma a Promising Treatment In Severe Knee Osteoarthritis?

Ilker ILHANLI[1]*, Necip GUDER[2] and Esin AVCI[3]

[1] Department of Physical Medicine and Rehabilitation, School of Medicine, Giresun University, Giresun, Turkey.
[2] Physical Medicine and Rehabilitation State Hospital, Giresun, Turkey.
[3] Department of Statistics, Faculty of Science, Giresun University, Giresun, Turkey.

Accepted 23 July, 2015.

Although evidence is insufficient, due to being an autologous application with low risk, low cost and potential contribution to the improvement, PRP is emerging as a method to be investigated more. In this study, we aimed to assess the effectiveness of intra-articular platelet-rich plasma injection in knee osteoarthritis by comparing with physical therapy.
Seventy patients were included in this study. Patients were randomized into 2 groups; platelet rich plasma (n = 35) and physical therapy (n = 35). Staging of the knee osteoarthritis was made according to the Kellgren-Lawrence classification. At the beginning of treatment (first evaluation step), at the end of treatment (second evaluation step) and 3 months after the end of treatment (third evaluation step) range of motion, VAS pain, WOMAC, SF-36 and Beck depression inventory were investigated.
There were no difference between the groups according to demographic data. At the end of the treatment and 3 months after the end of the treatment, significant improvement in range of motion has been detected in both groups, pain was reduced significantly in both groups and when WOMAC scores were compared, improvement was observed in both groups. However, in comparison, at the second and third evaluation steps, improvement at the WOMAC scores of platelet rich plasma group was significantly better than the physical therapy group.
When we compare with physical therapy, platelet-rich plasma is seem to be a well tolerated application that shows encouraging clinical results in patients with knee osteoarthritis.

Keywords: Platelet-rich plasma, knee, osteoarthritis, physical therapy

INTRODUCTION

Incidence of osteoarthritis (OA) increases steadily with age, affects 12.1 % of the population from 25 to 74 years old and it is the primary cause of physical disability after 65 years old (Gobbi, 2012). Studies have shown that 10 % of the population older than 55 years old own knee pain (Gobbi, 2012). Many conservative treatment options, such as oral and topical non-steroidal anti-inflammatory drugs, intra-articular corticosteroids and hyaluronic acid (HA) have been used for the treatment of OA and have yielded short- term efficacy with local or systemic side effects (Gobbi, 2012). Because of the high cost of bone and cartilage pathologies importance of the preventive interventions and the therapeutic options that regenerate tissue homeostasis and retard progression to OA is increased (Gobbi, 2012). Platelet-rich plasma (PRP) is a promising therapeutic application. Inflammation and cell proliferation are the important phases of bone and soft tissue injuries. Due to the possible contribution to the healing process, it is important to investigate PRP method. PRP is based on obtaining a high concentration of platelets from a patient's own blood plasma and applying to the damaged area. Studies have shown that the clinical efficacy of PRP products is expected to increase to, at minimum, 2 to 6 fold of platelets count from baseline value (Gobbi, 2012). Platelet and the plasma include growth factors and cellular signal factors supporting

Corresponding Author's E-mail: ilkerilhanli@hotmail.com

homeostasis and wound healing (De Vos, 2010; Foster, 2009). PRP is being obtained from the patient's blood sample by centrifuge and is being applied to the damaged area. After application patient is received to a short resting period before rehabilitation. In animal models, application of PRP has been shown to promote cartilage healing (Milano, 2010).
In spite of the positive results, studies in humans are limited because of the study designs and the lack of number of subjects.

MATERIAL AND METHODS

Seventy patients were included in the study, which were diagnosed as bilateral knee osteoarthritis. Accordance with the requirements of ethical standards (Helsinki Declaration) and approval of the institution, patients were randomized by computer and divided into 2 groups; PRP (n=35) and physical therapy (PT, n=35). Patients' written consents were obtained. Demographic data (age, gender, duration of complaints, body mass index) was recorded and staging of the knee osteoarthritis was made according to the Kellgren-Lawrence classification (Kellgren and Lawrence, 1957). While three intra-articular injections with an interval of one week were applied to PRP group, standard physical therapy (Hot pack for 15 minutes, Short Wave Diathermy for 10 minutes, Trans-cutaneous Electrical Nerve Stimulation for 15 minutes, stretching and strengthening exercises with 10 repeats, 500mg acetaminophen as rescue medication) was applied to the PT group for 15 sessions (5 sessions per week for 3 weeks).
After extraction of 15 ml of peripheral blood, the sample was centrifuged for 9 minutes at 3500 revolutions per minute. We obtained 6 ml of PRP and we proceeded to the intra-articular infiltration under sterile aseptic conditions. Before every injection, calcium- chloride was added to the PRP concentrate to activate platelets for inducing rapid formation of fibrin clot. Patients were instructed to avoid the use of co- interventions within the follow-up period. Acetaminophen (500 mg) could be used as rescue medication. After the injection, patients were sent home with instructions to limit the use of the leg for at least 24 hours and to use cold therapy for pain. After the third injection stretching exercises were allowed and one month after the end of injections, patients were recommended to begin strengthening program as tolerated. Injections were applied by the same physician (N.G.) and the physician who has collected the data (Self-administrated questionnaires were fulfilled by the patients and were sent to the physician I. I. for calculating the scores) was blind as well as the statistician.
In 3 steps; at the beginning of treatment, at the end of treatment and 3 months after the end of treatment range of motion (ROM) measurements, pain in activity, rest and sleep with visual analog scale (VAS), interrogation of daily living activities with Western Ontario And McMaster Universities (WOMAC) (Bellamy, 1988), and Short Form-36 (SF-36) questionnaires (Ware and Sherbourne, 1992), interrogation of depression with Beck questionnaire (Beck, 1961) were administered to the patients.
Exclusion criteria were age >80 years, Kellgren- Lawrence score < 3, systemic disorders such as diabetes, rheumatoid arthritis, hematological diseases (coagulopathy), severe cardiovascular diseases, infections, immunodefiency, use of anticoagulants or anti-aggregants, use of non-steroidal anti-inflammatory drugs in 5 days before and during treatment and hemoglobin values <11 g /dl, and platelet values <150,000 /mm^3.

Statistical analysis

In this study, data analysis was made with SPSS 21 software package. For gender, difference between patients treated with PRP, and PT was tested by chi-square. Difference between treatment groups according to variables respectively, age, body mass index, duration of complaints, stage of OA was tested with the independent two-sample t-test. For repeated measures Repeated-measures ANOVA was used. For ROM, VAS, Beck and mental score of SF-36 at first, second and third evaluation steps, difference between treatment groups was tested with nonparametric Friedman test due to not providing assumption of normality. To determine in which evaluation step the differences were occurred, nonparametric Benferroni-corrected Wilcoxon signed rank test was used. For WOMAC and physical score of SF -36, to test whether there is a difference between first, second and third evaluation steps, due to ensuring assumption of normality parametric two-way ANOVA test was utilized. To determine in which evaluation step the differences were occurred, the multiple comparison tests were used and to determine whether there were differences between treatment groups parametric t test was used. P values less than 0.05 were considered statistically significant.

RESULTS

Four patients from PRP group, and 2 patients from PT group didn't complete the treatment and were excluded from the study. Statistical analysis was made for 64 subjects (For PRP group n=31, and for PT group n=33).
There were no difference between the groups in terms of age (64.45±1.69 years for PRP group and 66.79±1.39 years for PT group, p=0.285), gender (26 females, 5 males in PRP group and 29 females, 4 males in PT group, p=0.729), body mass index (31.20±0.86 for PRP group and 32.18±0.95 for PT group, p=0.452) and duration of complaints (8.65±0.90 years for PRP group and 10.91±0.88 years for PT group, p=0.078). According to Kellgren- Lawrence score, 54.7% of patients had stage 3 OA (21 patients in PRP group and 14 patients in PT group) and 45.3% stage 4 (10 patients in PRP group and 19 patients in PT group).
Total number of platelets in the PRP per ml represented a mean increase of 2.2 - 2.6 times compared with whole blood values. In the plasma, presence of leukocytes was also observed, with a concentration of 1.3 times with respect to the normal blood value.
When we evaluated the patients at the end of treatment (second evaluation step) and 3 months after the end of treatment (third evaluation step), statistically significant improvement in ROM has been detected in both PRP and PT groups ($p<0.05$, Table 1). However, ROM was significantly better in PRP group than the PT group at all evaluation steps (Table 1). In both groups, improvement at the third evaluation step was more than the second evaluation step ($p<0.05$, Table1).
Before the treatment, VAS at activity and at rest were significantly higher in PRP group than the PT group (Table 1). At the second and third evaluation steps VAS at activity, at rest and at sleep showed significant improvement in both treatment groups. Improvement at the third evaluation step was greater than the improvement at the second step ($p<0.05$, Table1).
When WOMAC scores were compared, improvement was observed in both treatment groups (p=0.000, Table 1). However, in comparison, at the second and third evaluation steps, improvement at the WOMAC scores of PRP group was

significantly better than the PT group (p=0.004, p=0.000, respectively), (Table 1).

Before the treatment, at the end of treatment and at 3 months after the end of treatment, Beck scores of PRP group were significantly higher than the PT group (Table 1). However, according to Beck scores, an improvement was observed only in PRP group at 3 months after the end of treatment (p=0.042, Table 1), where there were no difference between the first evaluation step and second evaluation step (p=0.066, Table 1). In PT group, according to Beck scores, there were no difference between the start of treatment and other evaluation steps (p=0.165, Table 1).

According to physical score of SF- 36, we found no difference between treatment groups for the evaluation steps (p=0.460, p=0.282, p=0.303, respectively, Table 1). However, when we evaluated each treatment group itself, compared to baseline we found significant improvement at the end of treatment and 3 months after the end of treatment (p=0.000, Table 1).

For the mental score of SF- 36, both treatment groups did not differ between evaluation steps (p=0.727 for the PRP group and p=0.089 for the PT group), so we didn't calculate p values to find where the differences were. However, before the treatment and after the end of treatment, we found mental score of SF-36 significantly higher in PT group than the PRP group, where there were no differences at 3 months after the end of treatment.

In both groups we observed no complications or adverse effects of the treatment modalities.

DISCUSSION

There are some limitations in this study. Although, subject number was calculated to be 62 to achieve a 80% power of study and 64 patients completed the treatment, number of subjects should be more and the follow-up period should be much longer than 3 months. An objective assessment method, like measuring the cartilage thickness should be added, too. But, we have to keep in mind that, for these measurements a long follow-up period is needed.

PRP has been a promising treatment method for early osteoarthritis and chondropathies with an increasing use (Filardo and Kon, 2012). But yet, the effect of PRP treatment in severe knee OA is not well known. Platelets are rich of platelet growth factors, cytokines, chemokines and other mediators (Foster, 2009; Sanchez, 2003; Mishra, 2009; Anitua, 2004; Senet, 2003; Woodell-May, 2011). In vitro and in vivo animal studies have showed the potential impact of PRP on cellular anabolism and tissue regeneration (Kon, 2011; Torricelli, 2011).

In a study, it has been reported that after one year follow-up, PRP application reduced pain, improved function and delayed the progression of the disease in 73% of patients with knee osteoarthritis (Halpern, 2013). Sampson et al. (2010) reported significantly reduced pain and improved function in a small group of knee OA patients, with PRP injections after one year follow-up. Similar to these reports, in our study, significantly reduced pain and improved function was seen in the PRP group.

In a study conducted by Patel et al. one time PRP injection and two times PRP injections were compared with saline injection. PRP groups improved significantly, respect to the saline group. While there were no significant differences between the PRP groups, 6 months after treatment, in both groups, a slight setback in wellbeing of patients was detected (Patel, 2013).

Similar to our study, Wang-Saegusa et al. (2011) reported improvement of VAS, SF-36 and WOMAC scores after 6 months follow-up, in 261 patients with OA, who had three intra-articular injections of PRP with 2 week intervals. They reported no adverse effects related to PRP infiltration, as well as our findings.

Also, some studies, which compared the effectiveness of PRP and HA with WOMAC in knee osteoarthritis, have showed that PRP was more effective than HA (Spaková, 2012; Cerza, 2012).

In a study, PRP treatment was found effective in knee osteoarthritis at every age and every stage, but better results are reported especially at young age and early cartilage damage (Filardo, 2012). We investigated the efficacy of PRP in stage 3 and 4 knee OA, and found PRP method effective similar to this study. In another study by the same researchers, at 2 years follow-up of patients, although patients were significantly better than the baseline, they were worse than the evaluation in 12th month. Average duration of clinical improvement was 9 months and it was emphasized that the results were better in younger patients (Filardo, 2011). We found the improvement better after 3 months from the end of treatment and mean age was 64.45±1.69 in our patients. Unfortunately, our follow-up period was shorter than these studies and we don't know whether the clinical improvement will continue or not, along the following months; but, we thought that PRP treatment can improve the functions and reduce the pain in older patients with severe knee OA. Also, we have to keep in mind that, exercise program applied to the patients in PRP group may contributed to the well being. However, in a study including 65 patients suffering from OA, who were treated with intra-articular PRP injection, authors stated that, increasing age and developing degeneration result in a decreased potential for PRP injection treatment (Jang, 2013). Also, in a study conducted with 2 groups, with and without surgical treatment, Gobbi et al. reported statistically significant improvement by PRP treatment and suggested that, it provides early return to former activities (Gobbi, 2012).

In our study, improvement in WOMAC scores was better in PRP group than PT group. Also, improvement in depression scores was better, too. After injections, there is a 2 days period in which patients are experiencing considerable pain and subsequent relief. So, the injection procedures are painful experiences getting the patient's attention. These may all contribute to break depressive thought processes. After this painful period, abrupt decrease in pain may cause Pollyanna effect, that could be described as "everything would be much better" and may cause subsequent improvement in functional scores. It was the first treatment experience for each patient, both in PRP and PT groups, so we thought that, they approached to the treatment modalities out of regard.

Although evidence is insufficient, due to being an autologous application with low risk, low cost and potential contribution to the improvement, PRP is emerging as a method to be investigated more.

Table Legends

Table1. Differences between the evaluation steps for flexion of knee, WOMAC, VAS, SF-36 and BECK scores, and comparison of PRP versus PT.

	Evaluation steps	PRP (mean±SD)	Comp.	P- value	Evaluation steps	PT (mean±SD)	Comp.	P- value	PRP vs PT	P-value
Flexion(Right knee, degrees)	**a**	110,29±7,69	**a-b**	0,003	**a**	99,09±10,04	**a-b**	0,000	**a-a**	0,000
	b	111,77±7,03	**b-c**	0,000	**b**	102,42±9,77	**b-c**	0,000	**b-b**	0,000
	c	114,16±7,09	**a-c**	0,001	**c**	107,27±9,44	**a-c**	0,000	**c-c**	0,002
Flexion(Left knee, degrees)	**a**	111,29±7,11	**a-b**	0,011	**a**	100,45±10,18	**a-b**	0,000	**a-a**	0,000
	b	112,29±7,02	**b-c**	0,000	**b**	103,48±9,39	**b-c**	0,000	**b-b**	0,000
	c	114,23±7,38	**a-c**	0,003	**c**	108,79±9,10	**a-c**	0,000	**c-c**	0,011
WOMAC	**a**	67,13±1,85	**a-b**	0,000	**a**	67,85±1,65	**a-b**	0,000	**a-a**	0,772
	b	41,81±2,03	**b-c**	0,000	**b**	51,27±2,41	**b-c**	0,000	**b-b**	0,004
	c	24,65±2,55	**a-c**	0,000	**c**	38±2,06	**a-c**	0,000	**c-c**	0,000
VAS activity	**a**	8,84±1,10	**a-b**	0,000	**a**	8,27±1,10	**a-b**	0,000	**a-a**	0,044
	b	6,42±1,34	**b-c**	0,000	**b**	6,45±1,28	**b-c**	0,000	**b-b**	0,915
	c	3,03±1,97	**a-c**	0,000	**c**	4,12±1,78	**a-c**	0,000	**c-c**	0,024
VAS rest	**a**	5,61±1,86	**a-b**	0,000	**a**	2,67±1,81	**a-b**	0,000	**a-a**	0,000
	b	3,32±1,70	**b-c**	0,000	**b**	1,39±1,34	**b-c**	0,000	**b-b**	0,000
	c	1,16±1,46	**a-c**	0,000	**c**	0,55±1,03	**a-c**	0,000	**c-c**	0,055
VAS sleep	**a**	6,87±1,86	**a-b**	0,000	**a**	6,55±2,48	**a-b**	0,000	**a-a**	0,556
	b	4,06±1,79	**b-c**	0,000	**b**	4,42±1,98	**b-c**	0,000	**b-b**	0,450
	c	1,45±1,67	**a-c**	0,000	**c**	2,55±2,21	**a-c**	0,000	**c-c**	0,030
SF36 MCS	**a**	40,45±9,15	**a-b**	No difference p=0.727, didn't calculated	**a**	47,13±10,97	**a-b**	No difference p=0.089, didn't calculated	**a-a**	0,013
	b	41,15±9,32	**b-c**		**b**	47,78±10,24	**b-c**		**b-b**	0,010
	c	41,74±8,85	**a-c**		**c**	45,98±9,29	**a-c**		**c-c**	0,064
SF36 PCS	**a**	27,30±6,56	**a-b**	0,000	**a**	25,70±8,86	**a-b**	0,000	**a-a**	0,460
	b	31,29±7,56	**b-c**	0,000	**b**	28,83±9,06	**b-c**	0,000	**b-b**	0,282
	c	37,91±9,5	**a-c**	0,000	**c**	35,73±8,36	**a-c**	0,000	**c-c**	0,303
BECK	**a**	13,81±11,05	**a-b**	0,066	**a**	5,27±6,22	**a-b**	No difference p=0.165, didn't calculated	**a-a**	0,000
	b	13,32±10,79	**b-c**	0,018	**b**	5,24±6,04	**b-c**		**b-b**	0,000
	c	12,19±9,58	**a-c**	0,042	**c**	5,06±5,95	**a-c**		**c-c**	0,001

PRP: Platelet-Rich Plasma, **PT:** Physical Therapy, **SD:** Standard Deviation, **WOMAC:** WOMAC score, **VAS:** Visual Analog Scale, **SF-36 MCS:** Short Form-36 Mental Component Score, **SF-36 PCS:** Short Form-36 Physical Component Score, **BECK:** Beck Depression Inventory Score, **a:** Before the treatment, **b:** After the treatment, **c:** 3 months after the treatment, **a-b:** Comparison of the evaluations before the treatment and at the end of the treatment, **b-c:** Comparison of the evaluations at the end of the treatment and 3 months after the treatment, **a-c:** Comparison of the evaluations before the treatment and 3 months after the treatment, **Comp.:** Comparisons of evaluation steps, **PRP vs PT:** PRP versus PT.

CONCLUSIONS

PRP seems to be a well tolerated therapeutic application that shows encouraging clinical result in patients with stage 3 and 4 knee OA and may be more effective than the physical therapy. Standardization of PRP protocols, long-term follow-up and prospective, blinded, randomized studies should clarify questions regarding PRP effectiveness and durability of clinical improvement.

ACKNOWLEDGMENTS: None

REFERENCES

Gobbi A, Karnatzikos G, Mahajan V, Malchira S (2012). Platelet-rich plasma treatment in symptomatic patients with knee osteoarthritis: preliminary results in a group of active patients. Sports Health. 4:162-172.

De Vos RJ, Weir A, van Schie HT, Bierma-Zeinstra SM, Verhaar JA, Weinans H, Tol JL (2010). Platelet-rich plasma injection for chronic Achilles tendinopathy: a randomized controlled trial. JAMA. 303:144-149.

Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA (2009). Platelet-rich plasma: from basic science to clinical applications. Am J Sports Med. 37:2259-2272.

Milano G, Sanna Passino E, Deriu L, Careddu G, Manunta L, Manunta A, Saccomanno MF, Fabbriciani C (2010). The effect of platelet rich plasma combined with microfractures on the treatment of chondral defects: an experimental study in a sheep model. Osteoarthritis Cartilage. 18:971-980.

Kellgren JH, Lawrence JS (1957). Radiological Assessment of Osteoarthritis. Ann Rheum Dis. 16:494-501.

Bellamy N, Buchanan WW, Goldsmith CH, Stitt LW (1988). Validation of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol. 15:1833-1840.

Ware JE, Sherbourne CD (1992). The MOS 36-item Short Form Healthy Survey. I. Conceptual Framework and item selection. Med Care.

Beck AT (1961). An inventory for measuring depression. Arch Gen Psychiatry. 4:561-571.

Filardo G, Kon E: PRP (2012). more words than facts. Knee Surg Sports Traumatol Arthrosc. 20:1655-1656.

Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA (2009). Platelet-rich plasma: from basic science to clinical applications. Am J Sports Med. 37:2259-2272.

Sanchez AR, Sheridan PJ, Kupp LI (2003). Is platelet-rich plasma the perfect enhancement factor? A current review. Int J Oral Maxillofac Implants. 18:93-103.

Mishra A, Woodall J Jr, Vieira A (2009). Treatment of tendon and muscle using platelet-rich plasma. Clin Sports Med. 28:113-125.

Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT (2004). Autologous platelets as a source of proteins for healing and tissue regeneration. Tromb Haemost. 91:4-15.

Senet P, Bon FX, Benbunan M, Bussel A, Traineau R, Calvo F, Dubertret L, Dosquet C (2003). Randomized trial and local biological effect of autologous platelets used as adjuvant therapy for chronic venous leg ulcers. J Vasc Surg. 38:1342-1348.

Woodell-May J, Matuska A, Oyster M, Welch Z, O'Shaughnessey K, Hoeppner J (2011). Autologous protein solution inhibits MMP-13 production by IL-1beta and TNFalpha-stimulated human articular chondrocytes. J Orthop Res. 29:1320-1326.

Kon E, Filardo G, Di Martino A, Marcacci M (2011). Platelet-rich plasma (PRP) to treat sports injuries: evidence to support its use. Knee Surg Sports Traumatol Arthrosc. 19:516-527.

Torricelli P, Fini M, Filardo G, Tschon M, Pischedda M, Pacorini A, Kon E, Giardino R (2011). Regenerative medicine for the treatment of musculoskeletal overuse injuries in competition horses. Int Orthop. 35:1569–1576.

Halpern B (2013). PRP treatment potential for knee osteoarthritis. Clinical Journal of Sports Medicine. Hospital for Special Surgery New York, February 12. (http://www.hss.edu/newsroom_prp-treatment-potential-for-knee-osteoarthritis.)

Sampson S, Reed M, Silvers H, Meng M, Mandelbaum B (2010). Injection of platelet-rich plasma in patients with primary and secondary knee osteoarthritis: a pilot study. Am J Phys Med Rehabil. 89:961-969.

Patel S, Dhillon MS, Aggarwal S, Marwaha N, Jain A (2013). Treatment with platelet-rich Plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. Am J Sports Med. 41:356-364.

Wang-Saegusa A, Cugat R, Ares O, Seijas R, Cusco X, Garcia-Balletbo M (2011). Infiltration of plasma rich in growth factors for osteoarthritis of the knee short-term effects on function and quality of life. Arch Orthop Trauma Surg. 131:311-317.

Spaková T, Rosocha J, Lacko M, Harvanová D, Gharaibeh A (2012). Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil. 91:411-417.

Cerza F, Carnì S, Carcangiu A, Di Vavo I, Schiavilla V, Pecora A, De Biasi G, Ciuffreda M (2012). Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. Am J Sports Med. 40:2822-2827.

Filardo G, Kon E, Pereira Ruiz MT, Vaccaro F, Guitaldi R, Di Martino A, Cenacchi A, Fornasari PM, Marcacci M (2012). Platelet-rich plasma intra-articular injections for cartilage degeneration and osteoarthritis: single- versus double-spinning approach. Knee Surg Sports Traumatol Arthrosc. 20:2082-2091.

Filardo G, Kon E, Buda R, Vaccaro F, Guitaldi R, Di Martino A, Cenacchi A, Fornasari PM, Giannini S, Marcacci M (2011). Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 19:528-535.

Jang SJ, Kim JD, Cha SS (2013). Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. Eur J Orthop Surg Traumatol. 23:573-580.