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PLATELET-RICH PLASMA *VERSUS* HYALURONIC ACID FOR TREATMENT OF KNEE OSTEOARTHRITIS

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Abstract :
BACKGROUND: Platelet-rich plasma (PRP) and hyaluronic acid have been shown to be useful in the treatment of knee osteoarthritis. However, investigations comparing the efficacy of these two drugs together are insufficient.
AIM: To compare the outcomes of PRP *vs* hyaluronic acid injections in three groups of patients with bilateral knee osteoarthritis.
METHODS: This randomized controlled trial study involved 95 patients. Thirty-one subjects received a single injection of PRP (group PRP-1), 33 subjects received two injections of PRP at an interval of 3 wk (group PRP-2) and 31 subjects received three injections of hyaluronic acid at 1-wk intervals (group hyaluronic acid). The patients were investigated prospectively at the enrollment and at 4-, 8- and 12-wk follow-up with the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Scale questionnaires.
RESULTS: Percentages of patients experiencing at least a 30% decrease in the total score for the WOMAC pain subscale from baseline to wk 12 of the intervention were 86%, 100% and 0% in the groups PRP-1, PRP-2 and hyaluronic acid, respectively ($P < 0.001$). The mean total WOMAC scores for groups PRP-1, PRP-2 and hyaluronic acid at baseline were 63.71, 61.57 and 63.11, respectively. The WOMAC scores were significantly improved at final follow-up to 42.5, 35.32 and 57.26, respectively. The highest efficacy of PRP was observed in both groups at wk 4 with about 50% decrease in the symptoms compared with about 25% decrease for hyaluronic acid. Group PRP-2 had higher efficacy than group PRP-1. No major adverse effects were found during the study.
CONCLUSION: PRP is a safe and efficient therapeutic option for treatment of knee osteoarthritis. It was demonstrated to be significantly better than hyaluronic acid. We also found that the efficacy of PRP increases after multiple injections.

Keywords: Platelet-rich plasma, Hyaluronic acid, Osteoarthritis, Knee, Pain

Introduction:

Osteoarthritis is the most common articular disease, and it is an important cause of disability in the elderly[1,2]. The knee is the most frequent joint affected by osteoarthritis[3]. Osteoarthritis is a multifactorial chronic disease that starts with breakdown of joint cartilage and leads to decrease in joint space, subchondral sclerosis, synovitis and peripheral osteophytes formation[4,5]. It was estimated that more than 10% of the people aged ≥ 60 years suffer from this disease, and it is a major expense for all healthcare systems[6,7]. Clinical manifestations of the disease include functional pain and joint stiffness. Morning stiffness usually lasts less than 30 min followed by gel phenomenon that is a transient joint stiffness due to short-term immobility[8,9].

Current treatments for osteoarthritis include non-pharmacologic treatment, such as physical activity[10-12], and pharmacologic treatment, such as non-steroidal anti-inflammatory drugs, glucocorticoids and hyaluronic acid. These treatments aim to decrease pain and inflammation, but these drugs have restricted and short-term effects on control of symptoms and the patient's quality of life[13,14]. Platelet-rich plasma (PRP) is a plasma that is prepared from each patient's own blood, and it has a higher platelet concentration in comparison to normal plasma. PRP injection is a simple, low cost and minimally invasive procedure that provides concentrated growth factors for use as an intra-articular injection[15]. These growth factors are said to stimulate the healing of cartilage and thus improve arthritis[16,17]. Some studies alluded to the potential effect of PRP in treatment of chronic tendonitis, tennis elbow, chronic rotator cuff tendinopathy, jumper's knee, acute Achilles tendon rupture, muscle rupture, osteochondritis and osteoarthritis and meniscus repair[18-22]. The positive effects of PRP in improvement of knee osteoarthritis have been reported in some studies[23-26]. Studies have reported the effects of PRP on the proliferation of mesenchymal root cells and their chondrocyte differentiation in an *in vitro* environment[27,28], but evidence about the clinical use of PRP in the treatment of knee osteoarthritis is still insufficient.

Hyaluronic acid is a polysaccharide compound that includes glucuronic acid and acetylglucosamine. In osteoarthritis, the concentration and molecular weight of hyaluronic acid are reduced, and this is the basis of hyaluronic acid injection. Hyaluronic acid provides viscoelasticity of synovial fluid and stimulates formation of endogenous hyaluronic acid[29,30]. In addition to its effects on viscoelasticity, hyaluronic acid may be effective for the treatment of osteoarthritis by biochemical effects, such as stimulation of formation and accumulation of proteoglycan, inhibition of inflammatory mediators and analgesic effect[29,31,32]. However, because there are inadequate data on the effects of either different doses of PRP or hyaluronic acid in patients with osteoarthritis, we aimed in this study to compare the therapeutic efficacy of intra-articular injection of two different doses of PRP *versus* hyaluronic acid in the management of patients with osteoarthritis of the knee.

Methods :

This single-blinded parallel randomized controlled trial study was conducted on patients aged 40- to 80-years-old with knee osteoarthritis who were referred in 2020 .

The inclusion criteria were as follows: (1) patients with diagnosis of knee osteoarthritis as defined by the criteria of the American College of Rheumatology[33]; (2) patients who were staged using the Ahlback radiological grading; (3) patients having bilateral knee osteoarthritis with the same Ahlback grade; and (4) all knees with full range of motion.

The exclusion criteria were as follows: (1) history of diabetes; (2) history of other joint diseases in the knee, such as rheumatoid arthritis or gout; (3) history of knee surgery; (4) history of knee fracture; (5) intra-articular injection of corticosteroids during the previous 2 wk; (6) intra-articular injection of other drugs, such as hyaluronic acid over the previous 1 year; (7) contraindications for intra-articular injection, such as thrombocytopenia, coagulopathy, articular infection of knee, skin infection in the injection site, impairment of immunity (*e.g*., acquired immune deficiency syndrome or receiving immunosuppressive medication) and severe intra-articular effusion (in this case, intra-articular injection was started after treatment and cure of effusion); and (8) patients with Ahlback grade 3 or more.

All of the patients were examined by the senior orthopedic surgeon, who was blinded to the intervention groups. Plain radiographs were then taken of the knees with anterior-posterior and lateral views. Drug treatments (such as non-steroidal anti-inflammatory drugs, corticosteroids and other anti-inflammatory drugs) and non-drug treatments (knee physiotherapy with modalities, such as transcutaneous electrical nerve stimulation, laser, *etc*) were stopped for the 48 h before study interventions.

Ahlback radiological grading of knee osteoarthritis is classified as follows[34,35]: I: joint space narrowing < 3 mm; II: joint space obliterated or almost obliterated; III: minor bone attrition (< 5 mm); IV: moderate bone attrition (5–15 mm); and V: severe bone attrition (> 15 mm).

Results

A total of 129 patients were screened initially, of whom 34 were excluded due to failing to meet inclusion criteria or declining to participate. Finally, 95 patients underwent randomization. The flow of subjects from evaluation to participation is shown in the Consolidated Standards of Reporting Trials diagram . Three patients from group PRP-1, five patients from group PRP-2 and four patients from group hyaluronic acid were lost during follow-up. Hence, the final study population for analysis contained 28 patients in groups PRP-1 and PRP-2 and 27 patients in group hyaluronic acid.

There were no significant differences between the groups in age, gender, height, weight, BMI, Ahlback grading, WOMAC score and VAS pain score.

Analysis of the primary outcome showed that the response rate to a single dose of PRP was 85.7% and to hyaluronic acid was 0% over the 12 wk of follow-up ($P < 0.001$). This significant difference was also observed when comparing first and second follow-up between the groups, and the two groups of PRP had a significantly higher response rate compared to the hyaluronic acid group. For group PRP-1, no significant differences were identified in the percentage of patients experiencing at least a 30% and/or 50% decrease in the summed score for the WOMAC pain subscale between knees with Ahlback grade 1 and 2 from baseline at each follow-up. It was observed for group II as well.

The mean scores for all WOMAC and VAS pain parameters decreased significantly in the three groups from baseline at wk 4. However, it started a slightly increasing trend thereafter. There were significant differences in percentage change in the mean scores from baseline to wk 4 between the three groups. Group PRP-2 had the highest decreases in the mean scores from baseline to wk 4, which were significantly higher than group PRP-1 and group hyaluronic acid. Group PRP-1 also had significant decreases in the mean scores in comparison with group hyaluronic acid at wk 4. Percentage change in the mean scores was highest in group PRP-2 compared with groups PRP-1 and hyaluronic acid and was significantly higher in group PRP-1 *versus* group hyaluronic acid at other follow-ups as well.

Among the patients with Ahlback grade 1, the percentage change in scores from baseline for VAS pain score and all WOMAC subscales at each follow-up was significantly higher for group PRP-2 in comparison with group PRP-1. These differences were also found in the patients with Ahlback grade 2.

Over the study period, no major adverse events or complications were observed in the patients, and mild worsening of pain was noted in seven patients in the PRP groups, which was resolved by doses of acetaminophen.

Discussion

In this study, we attempted to compare the clinical outcomes of PRP *versus* hyaluronic acid injections in patients with bilateral knee osteoarthritis. We divided patients with Ahlback grade 1 or 2 osteoarthritis into the three groups of single and double injection of PRP and three injections of hyaluronic acid. All the patients were followed-up for 3 mo. We used WOMAC and VAS pain scores to evaluate the clinical outcomes. We found that the efficacy of PRP (single or double

injection) and hyaluronic acid started from intervention and continued until wk 4 and then started to decrease until wk 12. In other words, the highest efficacy of PRP was seen in both groups at wk 4 with about a 50% decrease in the symptoms compared with about a 25% decrease for those who had received hyaluronic acid. The efficacy of PRP treatment was significantly greater than the hyaluronic acid group at all follow-up times. In addition, two injections of PRP were more effective at each follow-up than a single injection. We did not witness any major complications during the follow-up. No similar studies exist from our region. Therefore, these data are beneficial in this point as well.

Few studies have been published comparing these treatments for osteoarthritis of the knee. In a recent systematic review, which collected the data related to the studies comparing outcomes between PRP and hyaluronic acid interventions, the reported studies were mostly in agreement with our research, showing that PRP injection is more effective for the treatment of osteoarthritis of the knee, especially in patients with lower grades of arthritis[42]. Two articles did not show any superiority of treatment with PRP over hyaluronic acid[43,44]. In our investigation, the trend of efficacy of PRP was demonstrated to continue until the first month after treatment with a decline thereafter. However, there was still a significant difference in the mean scores between follow-ups and baseline. However, in the study by Cerza et al[45], this benefit continued until the last follow-up at mo 6 without an eventual decline in efficacy. The systematic review by Di et al[42], showed that PRP could improve the WOMAC score at a minimum of 24 wk. However, PRP had no benefit over the control group when assessed by other pain measures, such as the International Knee Documentation Committee, the Knee Injury and Osteoarthritis Outcome Score and VAS[42]. When reviewing the literature, it becomes clear that there are variations between the individual studies in terms of number of patients, grading of osteoarthritis (Kellgren-Lawrence[30,43-47] or Ahlback[48] classification), length of follow-up (variable between 6 mo[30,45,48] and 12 mo[43,44,46,47], outcome scores used (WOMAC, Lequesne[45-49], VAS, the Knee Injury and Osteoarthritis Outcome Score[15,30,44,48,49] and number of PRP injections (one[15], two[46], three[30,43,44,47,48] or four[45]). Hence, the results can only be compared with caution.

One of the mechanisms by which PRP could improve the osteoarthritis of the knee is reported to be its anti-inflammatory effect. It has been shown that PRP can decrease the pro-inflammatory cytokines of interleukin-1 beta and tumor necrosis factor-alpha[50]. Leukocytes in PRP have been thought to have a role in anti-inflammatory activity, immune regulation and promotion of angiogenesis[51]. However, potential harmful effects of leukocytes on cartilage regeneration through the NF-κB pathway (a major pathway involved in the pathogenesis of osteoarthritis) have also been noted[52]. Therefore, further experimental and clinical studies are needed to clarify this molecular mechanism of PRP against osteoarthritis. It has been demonstrated that inactivated PRP increased formation of bone and cartilage *in vitro* and *in vivo*. Non-activated PRP was also reported to have an anabolic effect on proliferation of mesenchymal stem cells[53]. In addition, thrombin activation of PRP has an inhibitory action on chondrogenesis and osteogenesis[54]. Growth factors in PRP potentially affect tissue repair and growth through immigration and cell proliferation, angiogenesis, collagen production and stimulation of articular cartilage anabolism. They may slow down the catabolic process and decrease the synovial membrane hyperplasia[55,56]. It was pointed out that plasma rich in growth factors may also decrease NF-kB activation[57]. Additionally, platelet-derived growth factor has been stated to promote chondrocyte proliferation and the maintenance of their hyaline-like phenotype[47]. Fibrin is another factor that exists in PRP, which is used as a network for the differentiation of root cells and biological glue[58,59].

One limitation of the present study is the lack of a control group that was treated with corticosteroids for comparison. The second one is the short-time period of study. Future studies with longer follow-up are suggested to evaluate long-term efficacy and potential compactions. We also propose that future studies use magnetic resonance imaging to assess and quantify cartilage regeneration, if costs and ethical issues allow.

In conclusion, the results of this study showed that PRP is a safe and efficient therapeutic option for treatment of early stages of knee osteoarthritis by reducing the symptoms and recovering articular

function. PRP was indicated to be significantly better than hyaluronic acid. We also found that the efficacy of PRP increases after multiple injections. More studies with longer follow-up and a double-blind comparison of PRP with corticosteroids are suggested for the future.

References

1. Migliore A, Giovannangeli F, Granata M, Laganà B. Hylan g-f 20: review of its safety and efficacy in the management of joint pain in osteoarthritis. Clin Med Insights Arthritis Musculoskelet Disord. 2010;3:55–68. [PMC free article] [PubMed] [Google Scholar]
2. Neogi T. The epidemiology and impact of pain in osteoarthritis. Osteoarthritis Cartilage. 2013;21:1145–1153. [PMC free article] [PubMed] [Google Scholar]
3. Wood AM, Brock TM, Heil K, Holmes R, Weusten A. A Review on the Management of Hip and Knee Osteoarthritis. Int J Chronic Dis. 2013;2013:845015. [PMC free article] [PubMed] [Google Scholar]
4. Chen D, Shen J, Zhao W, Wang T, Han L, Hamilton JL, Im HJ. Osteoarthritis: toward a comprehensive understanding of pathological mechanism. Bone Res. 2017;5:16044. [PMC free article] [PubMed] [Google Scholar]
5. Man GS, Mologhianu G. Osteoarthritis pathogenesis - a complex process that involves the entire joint. J Med Life. 2014;7:37–41. [PMC free article] [PubMed] [Google Scholar]
6. Zhang Y, Jordan JM. Epidemiology of osteoarthritis. Clin Geriatr Med. 2010;26:355–369. [PMC free article] [PubMed] [Google Scholar]
7. Bitton R. The economic burden of osteoarthritis. Am J Manag Care. 2009;15:S230–S235. [PubMed] [Google Scholar]
8. Abhishek A, Doherty M. Diagnosis and clinical presentation of osteoarthritis. Rheum Dis Clin North Am. 2013;39:45–66. [PubMed] [Google Scholar]
9. Herrero-Beaumont G, Roman-Blas JA, Bruyère O, Cooper C, Kanis J, Maggi S, Rizzoli R, Reginster JY. Clinical settings in knee osteoarthritis: Pathophysiology guides treatment. Maturitas. 2017;96:54–57. [PubMed] [Google Scholar]
10. Castrogiovanni P, Di Rosa M, Ravalli S, Castorina A, Guglielmino C, Imbesi R, Vecchio M, Drago F, Szychlinska MA, Musumeci G. Moderate Physical Activity as a Prevention Method for Knee Osteoarthritis and the Role of Synoviocytes as Biological Key. Int J Mol Sci. 2019:20, 511. [PMC free article] [PubMed] [Google Scholar]
11. Musumeci G, Castrogiovanni P, Trovato FM, Imbesi R, Giunta S, Szychlinska MA, Loreto C, Castorina S, Mobasheri A. Physical activity ameliorates cartilage degeneration in a rat model of aging: a study on lubricin expression. Scand J Med Sci Sports. 2015;25:e222–e230. [PubMed] [Google Scholar]
12. Szychlinska MA, Castrogiovanni P, Trovato FM, Nsir H, Zarrouk M, Lo Furno D, Di Rosa M, Imbesi R, Musumeci G. Physical activity and Mediterranean diet based on olive tree phenolic compounds from two different geographical areas have protective effects on early osteoarthritis, muscle atrophy and hepatic steatosis. Eur J Nutr. 2019;58:565–581. [PubMed] [Google Scholar]
13. Ringdahl E, Pandit S. Treatment of knee osteoarthritis. Am Fam Physician. 2011;83:1287–1292. [PubMed] [Google Scholar]
14. Reid MC, Shengelia R, Parker SJ. Pharmacologic management of osteoarthritis-related pain in older adults. Am J Nurs. 2012;112:S38–S43. [PMC free article] [PubMed] [Google Scholar]
15. 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;80:278–283. [PubMed] [Google Scholar]
16. Dhillon MS, Patel S, John R. PRP in OA knee - update, current confusions and future options. SICOT J. 2017;3:27. [PMC free article] [PubMed] [Google Scholar]
17. Glynn LG, Mustafa A, Casey M, Krawczyk J, Blom J, Galvin R, Hannigan A, Dunne CP, Murphy AW, Mallen C. Platelet-rich plasma (PRP) therapy for knee arthritis: a feasibility study

in primary care. Pilot Feasibility Stud. 2018;4:93. [PMC free article] [PubMed] [Google Scholar]
18. Mishra A, Woodall J, Jr, Vieira A. Treatment of tendon and muscle using platelet-rich plasma. Clin Sports Med. 2009;28:113–125. [PubMed] [Google Scholar]
19. Knop E, Paula LE, Fuller R. Platelet-rich plasma for osteoarthritis treatment. Rev Bras Reumatol Engl Ed. 2016;56:152–164. [PubMed] [Google Scholar]
20. Hamid MS, Yusof A, Mohamed Ali MR. Platelet-rich plasma (PRP) for acute muscle injury: a systematic review. PLoS One. 2014;9:e90538. [PMC free article] [PubMed] [Google Scholar]
21. Blanke F, Vavken P, Haenle M, von Wehren L, Pagenstert G, Majewski M. Percutaneous injections of Platelet rich plasma for treatment of intrasubstance meniscal lesions. Muscles Ligaments Tendons J. 2015;5:162–166. [PMC free article] [PubMed] [Google Scholar]
22. Andia I, Latorre PM, Gomez MC, Burgos-Alonso N, Abate M, Maffulli N. Platelet-rich plasma in the conservative treatment of painful tendinopathy: a systematic review and meta-analysis of controlled studies. Br Med Bull. 2014;110:99–115. [PubMed] [Google Scholar]
23. 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;41:356–364. [PubMed] [Google Scholar]
24. Filardo G, Kon E, Pereira Ruiz MT, Vaccaro F, Guitaldi R, Di Martino A, Cenacchi A, Fornasari PM, Marcacci M. Platelet-rich plasma intra-articular injections for cartilage degeneration and osteoarthritis: single- versus double-spinning approach. Knee Surg Sports Traumatol Arthrosc. 2012;20:2082–2091. [PubMed] [Google Scholar]
25. Meheux CJ, McCulloch PC, Lintner DM, Varner KE, Harris JD. Efficacy of Intra-articular Platelet-Rich Plasma Injections in Knee Osteoarthritis: A Systematic Review. Arthroscopy. 2016;32:495–505. [PubMed] [Google Scholar]
26. Görmeli G, Görmeli CA, Ataoglu B, Çolak C, Aslantürk O, Ertem K. Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. Knee Surg Sports Traumatol Arthrosc. 2017;25:958–965. [PubMed] [Google Scholar]
27. Rubio-Azpeitia E, Andia I. Partnership between platelet-rich plasma and mesenchymal stem cells: in vitro experience. Muscles Ligaments Tendons J. 2014;4:52–62. [PMC free article] [PubMed] [Google Scholar]
28. Stessuk T, Puzzi MB, Chaim EA, Alves PC, de Paula EV, Forte A, Izumizawa JM, Oliveira CC, Frei F, Ribeiro-Paes JT. Platelet-rich plasma (PRP) and adipose-derived mesenchymal stem cells: stimulatory effects on proliferation and migration of fibroblasts and keratinocytes in vitro. Arch Dermatol Res. 2016;308:511–520. [PubMed] [Google Scholar]
29. Altman RD, Manjoo A, Fierlinger A, Niazi F, Nicholls M. The mechanism of action for hyaluronic acid treatment in the osteoarthritic knee: a systematic review. BMC Musculoskelet Disord. 2015;16:321. [PMC free article] [PubMed] [Google Scholar]
30. Montañez-Heredia E, Irízar S, Huertas PJ, Otero E, Del Valle M, Prat I, Díaz-Gallardo MS, Perán M, Marchal JA, Hernandez-Lamas Mdel C. Intra-Articular Injections of Platelet-Rich Plasma versus Hyaluronic Acid in the Treatment of Osteoarthritic Knee Pain: A Randomized Clinical Trial in the Context of the Spanish National Health Care System. Int J Mol Sci. 2016;17 [PMC free article] [PubMed] [Google Scholar]
31. McArthur BA, Dy CJ, Fabricant PD, Valle AG. Long term safety, efficacy, and patient acceptability of hyaluronic acid injection in patients with painful osteoarthritis of the knee. Patient Prefer Adherence. 2012;6:905–910. [PMC free article] [PubMed] [Google Scholar]
32. Bowman EN, Hallock JD, Throckmorton TW, Azar FM. Hyaluronic acid injections for osteoarthritis of the knee: predictors of successful treatment. Int Orthop. 2018;42:733–740. [PubMed] [Google Scholar]
33. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria

Committee of the American Rheumatism Association. Arthritis Rheum. 1986;29:1039–1049. [PubMed] [Google Scholar]
34. Köse Ö, Acar B, Çay F, Yilmaz B, Güler F, Yüksel HY. Inter- and Intraobserver Reliabilities of Four Different Radiographic Grading Scales of Osteoarthritis of the Knee Joint. J Knee Surg. 2018;31:247–253. [PubMed] [Google Scholar]
35. Ahlbäck S. Osteoarthrosis of the knee. A radiographic investigation. Acta Radiol Diagn (Stockh) 1968;Suppl 277:7–72. [PubMed] [Google Scholar]
36. Nadrian H, Moghimi N, Nadrian E, Moradzadeh R, Bahmanpour K, Iranpour A, Bellamy N. Validity and reliability of the Persian versions of WOMAC Osteoarthritis Index and Lequesne Algofunctional Index. Clin Rheumatol. 2012;31:1097–1102. [PubMed] [Google Scholar]
37. Ebrahimzadeh MH, Makhmalbaf H, Birjandinejad A, Keshtan FG, Hoseini HA, Mazloumi SM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) in Persian Speaking Patients with Knee Osteoarthritis. Arch Bone Jt Surg. 2014;2:57–62. [PMC free article] [PubMed] [Google Scholar]
38. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP) Arthritis Care Res (Hoboken) 2011;63 Suppl 11:S240–S252. [PubMed] [Google Scholar]
39. Fadaizadeh L, Emami H, Samii K. Comparison of visual analogue scale and faces rating scale in measuring acute postoperative pain. Arch Iran Med. 2009;12:73–75. [PubMed] [Google Scholar]
40. Rowbotham MC. What is a "clinically meaningful" reduction in pain? Pain. 2001;94:131–132. [PubMed] [Google Scholar]
41. Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. Eur J Pain. 2004;8:283–291. [PubMed] [Google Scholar]
42. Di Y, Han C, Zhao L, Ren Y. Is local platelet-rich plasma injection clinically superior to hyaluronic acid for treatment of knee osteoarthritis? A systematic review of randomized controlled trials. Arthritis Res Ther. 2018;20:128. [PMC free article] [PubMed] [Google Scholar]
43. Filardo G, Di Matteo B, Di Martino A, Merli ML, Cenacchi A, Fornasari P, Marcacci M, Kon E. Platelet-Rich Plasma Intra-articular Knee Injections Show No Superiority Versus Viscosupplementation: A Randomized Controlled Trial. Am J Sports Med. 2015;43:1575–1582. [PubMed] [Google Scholar]
44. Filardo G, Kon E, Di Martino A, Di Matteo B, Merli ML, Cenacchi A, Fornasari PM, Marcacci M. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. BMC Musculoskelet Disord. 2012;13:229. [PMC free article] [PubMed] [Google Scholar]
45. Cerza F, Carnì S, Carcangiu A, Di Vavo I, Schiavilla V, Pecora A, De Biasi G, Ciuffreda M. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. Am J Sports Med. 2012;40:2822–2827. [PubMed] [Google Scholar]
46. Raeissadat SA, Rayegani SM, Hassanabadi H, Fathi M, Ghorbani E, Babaee M, Azma K. Knee Osteoarthritis Injection Choices: Platelet- Rich Plasma (PRP) Versus Hyaluronic Acid (A one-year randomized clinical trial) Clin Med Insights Arthritis Musculoskelet Disord. 2015;8:1–8. [PMC free article] [PubMed] [Google Scholar]
47. Vaquerizo V, Plasencia MÁ, Arribas I, Seijas R, Padilla S, Orive G, Anitua E. 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;29:1635–1643. [PubMed] [Google Scholar]

48. Sánchez M, Fiz N, Azofra J, Usabiaga J, Aduriz Recalde E, Garcia Gutierrez A, Albillos J, Gárate R, Aguirre JJ, Padilla S, Orive G, Anitua E. 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;28:1070–1078. [PubMed] [Google Scholar]
49. 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;25:485–492. [PubMed] [Google Scholar]
50. Cole BJ, Karas V, Hussey K, Pilz K, Fortier LA. Hyaluronic Acid Versus Platelet-Rich Plasma: A Prospective, Double-Blind Randomized Controlled Trial Comparing Clinical Outcomes and Effects on Intra-articular Biology for the Treatment of Knee Osteoarthritis. Am J Sports Med. 2017;45:339–346. [PubMed] [Google Scholar]
51. Everts PA, van Zundert A, Schönberger JP, Devilee RJ, Knape JT. What do we use: platelet-rich plasma or platelet-leukocyte gel? J Biomed Mater Res A. 2008;85:1135–1136. [PubMed] [Google Scholar]
52. Xu Z, Yin W, Zhang Y, Qi X, Chen Y, Xie X, Zhang C. Comparative evaluation of leukocyte- and platelet-rich plasma and pure platelet-rich plasma for cartilage regeneration. Sci Rep. 2017;7:43301. [PMC free article] [PubMed] [Google Scholar]
53. 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;91:411–417. [PubMed] [Google Scholar]
54. Han B, Woodell-May J, Ponticiello M, Yang Z, Nimni M. The effect of thrombin activation of platelet-rich plasma on demineralized bone matrix osteoinductivity. J Bone Joint Surg Am. 2009;91:1459–1470. [PubMed] [Google Scholar]
55. Kon E, Mandelbaum B, Buda R, Filardo G, Delcogliano M, Timoncini A, Fornasari PM, Giannini S, Marcacci M. Platelet-rich plasma intra-articular injection versus hyaluronic acid viscosupplementation as treatments for cartilage pathology: from early degeneration to osteoarthritis. Arthroscopy. 2011;27:1490–1501. [PubMed] [Google Scholar]
56. Leitner GC, Gruber R, Neumüller J, Wagner A, Kloimstein P, Höcker P, Körmöczi GF, Buchta C. Platelet content and growth factor release in platelet-rich plasma: a comparison of four different systems. Vox Sang. 2006;91:135–139. [PubMed] [Google Scholar]
57. van Buul GM, Koevoet WL, Kops N, Bos PK, Verhaar JA, Weinans H, Bernsen MR, van Osch GJ. Platelet-rich plasma releasate inhibits inflammatory processes in osteoarthritic chondrocytes. Am J Sports Med. 2011;39:2362–2370. [PubMed] [Google Scholar]
58. Dohan Ehrenfest DM, Andia I, Zumstein MA, Zhang CQ, Pinto NR, Bielecki T. Classification of platelet concentrates (Platelet-Rich Plasma-PRP, Platelet-Rich Fibrin-PRF) for topical and infiltrative use in orthopedic and sports medicine: current consensus, clinical implications and perspectives. Muscles Ligaments Tendons J. 2014;4:3–9. [PMC free article] [PubMed] [Google Scholar]
59. Borie E, Oliví DG, Orsi IA, Garlet K, Weber B, Beltrán V, Fuentes R. Platelet-rich fibrin application in dentistry: a literature review. Int J Clin Exp Med. 2015;8:7922–7929. [PMC free article] [PubMed] [Google Scholar]