Platelet-rich Plasma for Articular Cartilage Repair

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Abstract: Platelet concentrates have been gaining popularity for a number of applications in orthopedic surgery as a way to enhance both healing of various tissues and reduce pain. One major area of focus has been the effect of platelet-rich plasma (PRP) on stem cells and chondrocytes and the potential for PRP to enhance cartilage regeneration as well as reduce catabolic factors that lead to cartilage degradation. This article provides an up-to-date review of the current literature regarding the effect of PRP on articular cartilage and its use in the treatment of osteoarthritis. Basic science, animal, and human clinical investigations are presented. In general, PRP has been shown to promote chondrogenic differentiation in vitro and lead to enhanced cartilage repair during animal investigations. Human trials, mostly conducted in the form of injection into knees with osteoarthritis, have shown promise in a number of investigations for achieving symptomatic relief of pain and improving function.

Key Words: cartilage, platelet-rich plasma, articular, PRP

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Articular cartilage is an avascular and aneural structure with limited intrinsic healing capacity.[1] Scientists and clinicians have been working to develop methods to create or augment articular cartilage repair techniques so that recreation of hyaline-like articular cartilage in a previously injured area is possible. One area of focus for the augmentation of cartilage regeneration has been the use of platelet-rich plasma (PRP). PRP is the plasma component within whole blood that has been processed to contain a supraphysiologic concentration of platelets.[2] The impetus for the use of PRP derives from the variety of bioactive growth factors found within platelets.[3,4]

This article will focus on the use of PRP for articular cartilage repair. To serve as a background for understanding of the in vitro and clinical data, this paper will review the anabolic factors contained within PRP as well as the catabolic enzymes and their signaling pathways, which PRP may be acting upon. In addition, the most up-to-date in vitro, animal, and human studies investigating the role PRP has on articular cartilage restoration and regeneration will be presented.

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PLATELET GROWTH FACTORS AND CATABOLIC CYTOKINES

Platelets contain 3 types of granules (α, δ, and λ), with the α granules containing growth factors as well as other proteins important in the coagulation cascade.[5] In vivo, these growth factors and coagulation proteins are released upon platelet activation, which occurs when the cell is exposed to collagen or von Willebrand factor, leading to platelet aggregation. Alternatively, platelet activation can be stimulated with exposure to thrombin or calcium chloride ($CaCl_2$), a mechanism some commercial PRP products utilize.

There are a variety of factors stored within the α granules that promote cartilage matrix synthesis and may counteract the catabolic effect of a variety of cytokines. Those that have been shown to promote cartilage matrix synthesis and are located within the granules are: transforming growth factor β,[6] fibroblast growth factor,[7] and platelet-derived growth factor,[8] among many others.[9] These factors, contained within PRP, may act to inhibit the most notable catabolic cytokines acting on articular cartilage: interleukin-1β (IL-1β) and tumor necrosis factor α (TNF-α).[10,11] Other investigations have also implicated increased levels of IL-6 as a catabolic cytokine.[12,13] The production of the catabolic enzymes IL-1, IL-6, and TNF-α is under the control of transcription factor nuclear factor κB (NF-κB), a family of proteins that regulates a wide range of stress-like inflammatory responses.[14–16] Although PRP does not act directly on NF-κB, the factors stored within α granules and released with platelet activation may act to counteract the downstream effects of NF-κB–mediated cartilage degradation. One of the goals of ongoing research in this area is to determine whether the factors contained within PRP may stimulate both chondrogenic growth and differentiation, and in addition, ameliorate the catabolic effect of cytokines produced at the time of joint injury or as a result of osteoarthritis.[17,18]

IN VITRO LABORATORY INVESTIGATIONS

The first step in determining whether PRP may be useful for the treatment of cartilage deficiency is to examine the effect of platelet granule contents on chondrocytes in vitro. There have been a number of investigations which have examined this question (Table 1). Pereira and colleagues examined the effect of platelet lysate (PL) versus standard fetal calf serum (FCS) on the growth and matrix gene expression of human chondrocytes harvested at the time of total knee arthroplasty. They found that the PL-cultured cells doubled 5 times the rate of the FCS-cultured cells but that both cells lost the expression of type II collagen as the number of passages increased. After

TABLE 1. Investigations Examining the Effect of Platelet-rich Plasma (PRP) on Chondrocytes In Vitro

References	PRP Type	Chondrocyte Source	Cell Growth Characteristics With PRP	Cell Genetic Expression With PRP	Other Findings
Pereira et al[19]	PL	Human chondrocytes harvested at TKA	Cells cultured in PL had 5× the doubling rate vs. those in fetal calf serum; more fibroblastic shape in PL-cultured cells	At first passage (10 doublings), PL cells expressed type I collagen and SOX-9 with only trace amounts of type II collagen; FCS-cultured cells after 3 doublings lost type II collagen expression	NF-κB and COX expression significantly decreased with addition of PL to IL-1 containing cell culture vs. IL-1 cell culture alone
Van Buul et al[20]	Human PRP (Biomet GPS III)	Human chondrocytes harvested at TKA	—	PRP increased COL2A1 and aggrecan gene expression and decreased ADAMTS4 and PTGS2 expression	PRP downregulated NF-κB activity; addition of PRP did not increase GAG production nor inhibit NO synthesis
Kruger et al[21]	Human PRP (Caridian BCT)	Postmortem progenitor cells from tibia and femur	PRP-treated cells showed increased pellet density	Increase in type II collagen, aggrecan, and link protein production	Stimulatory effect also found with TGF-β3 and PRP + TGF-β3 vs. control human serum group
Park et al[22]	New Zealand white rabbit PRP	Chondrocytes from rabbit trochlea	Increased chondrocyte cell proliferation with PRP	Increased expression of SOX-9, aggrecan, TGF-β, and VEGF	—
Woodell-May et al[23]	Human PRP (Biomet GPS III)	Human knee chondrocytes	—	—	PRP significantly inhibited the production of MMP-13 induced by IL-1β and TNFα
Bendinelli et al[24]	Human PRP (Biomet GPS II)	Immortalized chondrocyte line	—	PRP decreased NF-κB activity and expression of COX-2 and CXCR4 genes	Method of NF-κB inhibition involves IkBα expression, (NF-κB-p65 subunit retention in the cytosol)
Akeda et al[25]	Porcine PRP (DePuy Symphony 2 Platelet Concentration System)	Mature porcine chondrocytes	Increased overall culture DNA content with PRP-cultured cells (vs. FBS)	Significant increase in PG and collagen synthesis in PRP group	—
Xie et al[26]	New Zealand white rabbit PRP	New Zealand white rabbit BMSC and ADSC	Increased MSC proliferation with PRP	Increased aggrecan, SOX-9, and type II collagen mRNA and protein with PRP	Elevated levels of chondrogenic mRNA in BMSC vs. ADSC
Mishra et al[27]	Human PRP (Medtronic Magellan)	Commercial human MSCs	Cell number of fibroblasts and $CD34^+$ cells increase in proportion to percent PRP applied	Significantly higher levels of Runx2, SOX-9, and aggrecan with PRP	20% PRP showed fewer $CD34^+$ cells vs. 5% PRP
Browning et al[28]	Human PRP (Harvest Smart PReP)	Human synovial fibroblasts	—	—	Significant increase in IL-1β, IL-6, MMP-1 and MMP-3 production with PRP

ADSC indicates adipose-derived stem cell; BMSC, bone marrow–derived stem cell; COL2A1, type II collagen (marker for hyaline cartilage); COX, cyclooxygenase (degradative enzyme); FBS, fetal bovine serum; FCS, fetal calf serum; GAG, glycosaminoglycans; IkBα, nuclear factor of kappa light polypeptide gene enhancer in B-cell inhibitor α; IL-1, interleukin-1; MMP, matrix metalloproteinase; MSC, mesenchymal stem cells; NFκB, nuclear factor kappa B (a transcription factor involved in cytokine production); NO, nitric oxide (catabolic free radical); PL, platelet lysate; PPP, platelet-poor plasma; PTGS2, prostaglandin-endoperoxide synthase 2 (degradative enzyme); TGF-β, transforming growth factor β; TKA, total knee arthroplasty; VEGF, vascular endothelial growth factor.

implantation into nude mice, the authors also found that chondrocytes expanded in the presence of PL and maintained their redifferentiation capacity longer than those cultured in FCS.[19] This was likely related to the finding of elongated SOX-9 expression in the PL-cultured cells as SOX-9 is a major transcription factor involved in chondrocyte differentiation.[29] In another study, van Buul et al[20] examined the effects of PRP on chondrocytes cultured in the presence of IL-1β, a common catabolic cytokine. They found that PRP diminished IL-1β-induced inhibition of type II collagen and aggrecan as well as reduced a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS) gene expression (Table 1).

In addition to chondrocytes, the effect of PRP on human mesenchymal stem cells has also been investigated (Table 1).[26,27] Xie et al harvested both bone marrow–derived stem cells (BMSC) and adipose-derived stem cells (ADSC) from New Zealand white rabbits.[26] For both the BMSC and ADSC, the cells were cultured in 3 experimental conditions: a control condition (expansion medium only), with 10% PRP drawn from the rabbits used in the investigation, or in cultures with known chondrogenic promoters. The PRP used had nearly 6 times the platelet concentration of whole blood. The amount of SOX-9, aggrecan, type I collagen, and type II collagen mRNA and protein was examined with real-time polymerase chain reaction and Western blot analysis. They found that the PRP treatment group demonstrated a 3- to 5-fold increase in the number of BMSC and ADSC after 7 days in culture compared with controls. In addition, the levels of mRNA and protein for SOX-9, aggrecan, and type II collagen were all increased in the PRP group as compared with control. Interestingly, BMSC showed a greater production of chondrogenic mRNA versus ADSC.[26] These results suggest that PRP may act as a stem cell growth promoter and chondrogenic differentiator when applied to both ADSC and BMSC.

In general, PRP typically increases cell growth, increases chondrocyte transcription of proteins, and decreases NF-κB–mediated production of catabolic cytokines (Table 1).[30] Browning et al,[28] however, investigated the effect of PRP on cultures of human synovial fibroblasts. Synovial tissue of patients undergoing routine knee arthroscopy was biopsied and cultured with and without autologous PRP. The synoviocytes cocultured with PRP [vs. platelet-poor plasma (PPP)] showed significantly increased levels of IL-1β and IL-6 as well MMP-1 and MMP-3, all implicated in chondrocyte catabolic metabolism. These findings are in contrast to those by Sundman et al[31] who reported that growth factor presence was significantly associated with platelet concentration.

ANIMAL STUDIES

At present, the use of PRP in articulate cartilage repair is still in its infancy, and as such, there remains a paucity of high level studies available in the literature to support its use. Several preclinical animal model studies have been described, however, with promising results. Of utmost importance when interpreting the results of animal or human clinical studies is truly understanding the PRP product being investigated, especially with regard to the actual platelet or leukocyte concentration being used, as these can vary from animal to animal and certainly from animal to human. A summary of these studies is presented in Table 2, including weaknesses of each study as they pertain to the results.

Sun et al[33] studied the effects of PRP in a rabbit model. In their study, osteochondral defects approximately 5 mm (diameter) by 4 mm (depth) were created and subsequently treated with either autogenous PRP in a poly-lactic-glycolic (PLGA) carrier versus PLGA alone. A control group of no treatment was also studied. The authors found that after 4 and 12 weeks of treatment, the PRP group had superior results compared with both groups with regard to neochondrogenesis in addition to other several outcomes. In a similar study, Milano et al[34] examined the effect of PRP in a sheep model. After creation of a full-thickness osteochondral defect into the medial femoral condyle, the authors compared the effect of microfracture alone, microfracture with PRP polymerized into the defect with thrombin, and microfracture with injection of unclotted PRP into the joint. At sacrifice 6 months after the treatment, the authors found improved results in the polymerized PRP group when compared with the other 2 groups. The authors also reported that histologic scores were higher for the 2 PRP groups compared with the microfracture only group.[34] Combined, these studies suggest that compared with control treatments, PRP is beneficial for chondrogenesis in the setting of osteochondral defects.

Conversely, in another sheep model, Kon et al[35] analyzed the effect of $CaCl_2$-activated PRP combined with a collagen scaffold on the ability to fill medial femoral condyle osteochondral defects, approximately 7 mm in diameter by 9 mm deep Sheep were randomized to either scaffold, scaffold loaded with PRP, and empty defect (control). Sacrifice occurred at 6 months after the surgery. Interestingly, the authors found impaired cartilage and bone repair properties by histology when compared with a group repaired with the scaffold alone (no PRP). In the control group, only fibrous tissue fill was seen (no bone or cartilage healing occurred). The authors concluded that not only did PRP not have an additive effect but rather it had a negative effect on osteochondral lesion repair by "disturbing the regenerative process."[35]

In a model examining osteoarthritis, Saito et al[36] used a rabbit model of anterior cruciate ligament transection. In this study, either PRP or PPP contained in gelatin hydrogels were injected intra-articularly at 3-week intervals beginning 4 weeks after transection. The authors reported that the PRP-treated rabbits had significantly decreased progression of osteoarthritis when compared with the PPP rabbits. The authors concluded that the release of growth factors within the PRP have preventative effects against osteoarthritis progression.

Recently in 2012, Serra et al[37] also used a rabbit model studying the effects of PRP on full-thickness articular cartilage defects. In this study, cartilage lesions were drilled into the medial femoral condyle followed by either injection of autologous PRP or physiologic saline (placebo). The authors found that at 19 weeks postoperatively, the control group was both microscopically and macroscopically superior with regard to defect filling, whereas the PRP group did not show better results compared with placebo. Both test groups showed characteristics of fibrocartilage fill, whereas neither produced a normal appearing hyaline-like cartilage.[37]

HUMAN CLINICAL STUDIES

As noted above, the preclinical animal model data has mixed results when it comes to the use of PRP in cartilage restoration. Human clinical studies are even less clear,

TABLE 2. Summary of Preclinical Animal Studies Analyzing Platelet-rich Plasma (PRP)

References	Type	Methods	PRP Characteristics	Conclusions	Weaknesses
Brehm et al[32]	Animal—goat	OCD of femoral trochlea treated with cartilage constructs secured with liquid, unclotted PRP "adhesive" vs. sutured periosteal flap alone	Platelet and leukocyte counts not reported	No difference in graft security or quality of cartilage construct	Only a total of 2 animals per group used (8 defects per joint) PRP classification not described
Sun et al[33]	Animal—rabbit	Trochlear groove OCD created, then treated with PRP (thrombin-activated) in PLGA carrier vs. PLGA alone vs. control group Sacrifice at 4 and 12 wk	Platelet (5.12× greater concentration compared with peripheral blood) but no leukocyte concentrations reported	PRP group with higher extent of neochondrogenesis, increased GAG production in ECM, more normal appearance of newly formed bone on micro-CT	Relatively short follow-up Platelet but no leukocyte concentrations reported
Milano et al[34]	Animal—sheep	Chronic MFC defects created during index procedure; then during second surgery 12 mo later, treated with MFX alone, MFX with PRP polymerized with thrombin (Ca-gluconate-clotted gel), or MFX with unclotted PRP Sacrifice at 6 mo (1.5 y following index surgery)	Platelet (4× greater concentration compared with peripheral blood) but no leukocyte concentrations reported	Improved results in PRP polymerized group; higher histologic scores for both PRP groups compared with MFX alone	Two procedures to create a "chronic" model, with unknown amount of reparative response (no analyses performed after index procedure) Relatively short follow-up Effect of PRP not isolated (because of MFX) Platelet but no leukocyte concentrations reported
Kon et al[35]	Animal—sheep	Ipsilateral MFC and LFC defects created, then treated either with scaffold only, scaffold with $CaCl_2$-activated PRP, or empty defect (control) Scaffold: multilayer hydroxyapatite collagen construct Sacrifice at 6 mo	Platelet (average 316 ± 36% yield compared with peripheral blood) but no leukocyte concentrations reported	Significantly improved cartilage/bone repair properties in scaffold alone group compared with PRP group Incomplete bone regeneration and irregular chondral surface integration in PRP group Histologic and immunohistochemical results also favoring non-PRP group	Use of ipsilateral, medial, and lateral femoral condyle defects makes it difficult to isolate either condyle's result Relatively short follow-up Platelet but no leukocyte concentrations reported
Saito et al[36]	Animal—rabbit	ACL transection followed by 3% PRP or 3% PPP injections twice every 3 wk starting at 4 wk postoperatively Injections contained in gelatin hydrogels (3% PRP in alginate bead) Sacrifice at 10 wk	Platelet but no leukocyte concentrations reported	PRP with significantly suppressed OA progression Significantly stimulated GAG synthesis in vitro and increased expression of PG core protein mRNA in the articular cartilage	Platelet but no leukocyte concentrations reported
Serra et al[37]	Animal—rabbit	MFC defects created and subsequently treated with injection of autologous PRP or saline (placebo) Injections given at the end of surgery, then every 2 d for 7 total injections All injections bilateral Control group of rabbits without any intervention Sacrifice at 16 or 19 wk	No platelet or leukocyte concentrations reported	Control group microscopically, macroscopically, and biomechanically superior to both placebo and PRP groups No differences between placebo and PRP groups at 19 wk	No platelet or leukocyte concentrations reported Relatively short-term follow-up No immunohistochemical analysis

ACL indicates anterior cruciate ligament; CT, computed tomography; ECM, extracellular matrix; GAG, glycosaminoglycans; LFC, lateral femoral condyle; MFC, medial femoral condyle; MFX, microfracture; OA, osteoarthritis; OCD, osteochondral defect; PLGA, poly-lactic-glycolic; PPP, platelet-poor plasma; PRP, platelet-rich plasma.

TABLE 3. Summary of Human Clinical Studies Analyzing Platelet-rich Plasma

References	No. Patients	Methods	PRP Characteristics	Conclusions	Weaknesses
Sanchez et al[38]	60	Retrospective cohort study on treatment for OA 30 patients with weekly PGRF injections and 30 patients with weekly HA injections for a total of 3 wk	Venous blood drawn and centrifuged Plasma fraction above buffy coat aspirated into new tube, activated with $CaCl_2$, and injected before coagulation Platelet concentration: 2 ± 0.5× increase compared with peripheral blood WBC concentration: below the detection limit of the analyzer (absence of leukocytes) Other GF levels reported	At 5 wk after therapy, PRP group with statistically improved pain, function, and WOMAC scores	No use of image guidance Short-term follow-up No power analysis
Kon et al[39]	100	PRP for degenerative chondral lesions and OA All received 3 $CaCl_2$-activated PRP injections every 3 wk	Venous blood drawn and centrifuged twice to 20 mL Divided into units of 5 mL After first injection in office, other units stored at –30°C Platelet (600%) but no leukocyte concentrations reported	At 1 y, all outcomes improved compared with basal rates but worsened compared with 6 mo outcomes Younger patients with increased response (< 65 y old)	No use of image guidance No leukocyte concentration reported No control group
Sampson et al[40]	14	Prospective study on treatment for OA; total of 3 PRP injections weekly in 4-wk intervals	Venous blood drawn, mixed with citrate dextrose formula and centrifuged to 6 mL PRP PRP combined with 0.6 mL of thrombin suspension in a 10% $CaCl_2$ solution Injected into suprapatellar bursa under ultrasound guidance	Favorable outcomes at 12 mo (VAS, KOOS) 8/13 improved; 3/13 same; 2/13 worse	Small sample size No control group No platelet or leukocyte concentration reported
Kon et al[41]	150	Prospective comparative trial for treatment of OA 50 patients with 3 $CaCl_2$-activated PRP injections every 2 wk; 50 patients with high–molecular-weight HA injections; 50 patients with low–molecular-weight HA injections	Venous blood drawn and centrifuged twice to 20 mL Divided into units of 5 mL After first injection in office, other units stored at –30°C Platelet (600%) but no leukocyte concentrations reported	By 6 mo after therapy, improved results in PRP group with pain and symptoms; worse outcomes in older patients with more degenerative joints Worst results in high–molecular-weight HA group	No randomization Different protocol depending on the treatment center Unknown number of HA injections No use of image guidance No leukocyte concentration reported No control group
Filardo et al[42]	91	PRP for degenerative chondral lesions and OA All received 3 $CaCl_2$-activated PRP injections every 3 wk	Venous blood drawn and centrifuged twice to 20 mL Divided into units of 5 mL After first injection in office, other units stored at –30°C Platelet (600%) but no leukocyte concentrations reported	At 2 y, all outcomes improved compared with basal rates but worsened compared with 1 y outcome Median duration of improvement: 9 mo Better results in younger patients and patients with less degeneration	No use of image guidance No leukocyte concentration reported No control group
Patel et al[43]	78	Randomized double-blinded study with control group vs. single vs. 2 injections of PRP	Leukocyte filtered Testing of PRP before injection confirmed platelet concentration at least 3× baseline	Single or double PRP injection in knees with mild/moderate osteoarthritis produced improved WOMAC scores vs. saline injection control	Blinding may have been compromised as one PRP group received 2 injections, whereas control received only 1

BM-MSCs indicates bone marrow mesenchymal stem cells; $CaCl_2$, calcium chloride; KOOS, knee injury and osteoarthritis outcome score; OA, osteoarthritis; OCD, osteochondral defect; PR-FG, platelet-rich fibrin glue; PRP, platelet-rich plasma; VAS, visual analog scale; WBC, white blood cells; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

although recent clinical trials have shown the use of PRP for cartilage restoration in humans to be beneficial. A summary of these studies is presented in Table 3.

In 2010, Haleem et al[44] described the use of bone marrow–derived mesenchymal stromal cells (BM-MSCs, aspirated from the iliac crest) mixed with PRP and thrombin for the treatment of cartilage defects. This pilot study included 5 patients who underwent an initial aspiration of the BM-MSCs from the iliac crest, followed by surgical placement of the cells mixed with a platelet-rich fibrin glue secured by a sutured periosteal flap. At both 6-month and 1-year follow-up, clinical outcome scores as well as examinations using magnetic resonance imaging were significantly improved compared with preoperative values. The authors did report the platelet concentration of the PRP to be $7.7 \pm 1.1 \times 10^8$/mL but did not report on the leukocyte concentration of the mixture.

In one of the larger cohort studies available, Sanchez et al[38] reported on a prospective group of 60 patients with knee pain receiving either PRP or hyaluronic acid (HA) injections weekly for 3 weeks. Although this study did not specifically focus on the treatment of isolated chondral defects, this was one of the first comparison studies published describing the clinical effects of PRP therapy. Overall, the PRP group had statistically significantly improved pain scores, function scores, and overall Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores when compared with the HA group. Weaknesses of this study include a relatively short follow-up period (5 weeks) and no use of image guidance for the injections. Of note, the authors did report the platelet concentration of the PRP to be approximately 2.0 ± 0.5 times increased compared with that of the peripheral blood as well as a nondetectable leukocyte concentration.

In an even larger study, Kon et al[39] prospectively evaluated 100 patients treated with 4 intra-articular PRP injections given every 3 weeks. These patients had a wide range of diagnoses, including degenerative chondral lesions, early OA, and advanced OA. The authors reported an overall improved outcome with regard to quality of life, pain, and function when compared with pretreatment levels; however, results appeared to peak at the 6-month time point and worsen at 1 year. Further, younger patients had an increased response compared with older (> 65 y of age) patients. In this study, the authors described the platelet concentration of the PRP as 600% that of the peripheral blood but did not report on the leukocyte concentration. Further, there was no use of image guidance to guide the injection placement and there was no control group for comparison.

Patel et al[43] performed a double-blind randomized controlled trial investigating the effect of PRP versus saline injections in patients with early osteoarthritis of the knee. A total of 156 knees were divided into 3 groups: saline control group, a single injection of PRP, and 2 injections of PRP 3 weeks apart. White blood cell–filtered PRP with a concentration of platelets 3× baseline was used. The authors reported significantly improved WOMAC scores over baseline in both PRP groups at all time points during the 6-month follow-up. There was a deterioration in WOMAC scores from baseline in the saline injection group. Both PRP groups showed significant improvement when compared with the control saline group, with no significant difference in the WOMAC score noted between the 2 PRP groups. Results in the PRP group did deteriorate after 6 months. This was a well-conducted randomized double-blind control group study with testing the of PRP product for platelet count. Blinding, however, may have been an issue as patients receiving 2 injections may have known they were not in the control group.

Recently, Kon et al[41] published a prospective clinical study comparing the efficacy of PRP injections compared with HA injections for the treatment of cartilage degenerative lesions and OA. In this study, 50 patients received 3 autologous PRP injections every 2 weeks, 50 patients received high–molecular-weight HA injections, and 50 patients received low–molecular-weight HA injections. The authors used 2-month and 6-month end points and found that overall, at 6 months after therapy, improved results were seen in the PRP group with regard to pain and symptom control. The authors did report worse outcomes in patients who were older with more advanced arthritis.[41] Although the study was well designed and conducted, the authors did not use image guidance, randomize the patients, have a control group, and did not report on the leukocyte concentration of the PRP. The platelet concentration, however, was reported to be 600% that of the peripheral blood.

In one of the longer-term studies available, Filardo and colleagues reported on the 2-year follow-up of patients undergoing PRP injection for degenerative cartilage lesions and OA. This study was a longer-term follow-up on the previously described study by Kon and colleagues. A total of 114 knees (90 patients) were included for the review.[42] All patients received 3 intra-articular PRP injections as described above. The authors reported that all outcome measures including IKDC, VAS, and patient satisfaction worsened at the 2-year follow-up point, despite improvements across the board at 1 year. Overall, the authors concluded good efficacy of PRP in the short term but that more clinical and basic science work is needed to determine how to improve the clinical results. As noted above in the description of the index study, the platelet concentration of the PRP was 600% that of the peripheral blood, but the authors did not report on the leukocyte concentration. Further, there was no use of imaging to guide the injection placement and there was no control group for comparison.

Overall, preclinical animal model studies and early human clinical studies demonstrate positive effects of PRP on the treatment of articular cartilage disease. Nevertheless, more work is needed to determine appropriate patient selection and actual administration protocols with regard to the timing and delivery of the actual injections. Further, it remains unclear as to how promising the effects will stand up over time, and longer, prospective randomized trials are needed before being able to draw conclusions regarding the efficacy of PRP in the treatment of cartilage lesions.

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