CURRENT CONCEPT REVIEW

Intraarticular Injections of Platelet-rich Plasma (PRP) in the Management of Knee Osteoarthritis

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Abstract

The clinical use of PRP therapy in the practical setting of orthopaedic fields is increasing partly because of the accessibility of devices that are used in outpatient preparation and delivery. Another reason is the strong advertisement of PRP procedures as the ultimate treatment and novel technology for knee problems by a few orthopaedic surgeons based on claims of abundant scientific evidence. Hence, PubMed articles related to the clinical use of PRP in knee osteoarthritis were searched using the key words: PRP, knee and osteoarthritis in order to study these claims. A total of 20 reports were found directly related to the topic. The aforementioned clinical studies suggest that intraarticular injections of PRP could have preventive effects against osteoarthritis progression. However, presently there is no clear evidence from well-designed clinical trials that intraarticular injections of PRP are efficacious in osteoarthritis. Therefore, at this time the efficacy of PRP requires more investigation, wherein better scientific studies should be performed that include high powered randomized controlled trials.

Keywords: Platelet-rich Plasma (PRP), Knee, Osteoarthritis

Introduction

Platelet-rich plasma (PRP) is a concentrated extract of platelets from autologous blood, and is a possible treatment option for the stimulation and acceleration of regeneration in orthopaedics (1-3). The theoretical application of PRP in the stimulation and acceleration of soft-tissue healing and bone regeneration are topics of great interest for clinicians. Because platelets have a high concentration of factors and cytokines within their alpha granules and dense granules, this makes PRP an appealing therapeutic alternative. Several vital factors found inside the alpha granules of the platelet are platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-ь), insulin-like growth factor-1 (IGF-1), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF) among others (2). The dense granules of the platelet contain neuromodulators and inflammatory mediators such as histamine and serotonin. Platelets are stimulated to release these growth factors and cytokines by exposure either to collagen or to thrombin and calcium. All the aforementioned growth factors and cytokines may impact soft tissue healing and bone regeneration.

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Presently, the availability of devices for outpatient preparation and delivery contributes to the increased clinical use of PRP therapy in the practical setting of orthopaedic fields. In addition, a number of orthopaedic surgeons excessively promote PRP procedures as a decisive treatment and novel technology for the treatment of knee problems, which they claim to be supported by abundant scientific evidence (1).

The purpose of this review article was to summarize the existing knowledge on the role of PRP in knee osteoarthritis based on the studies published in PubMed from 2008 to July 2013. Key words PRP, knee and osteoarthritis were used in our search and consequently 20 reports were found directly related to the topic.

Studies on intraarticular injections of PRP in knee osteoarthritis

Sanchez et al. tried to obtain information about the effectiveness of intraarticular injections of an autologous preparation rich in growth factors (PRGF) for knee osteoarthritis treatment (4). They characterized PRGF treatment by platelet count and concentration of relevant growth factors (TGF-Beta1, PDGF-AB, VEGF-A; HGF and IGF-I)

involved in healing mechanisms. Additionally, they performed an observational retrospective clinical study using hyaluronan injections as a control. The observed success rates by week 5 for the pain subscale reached 33.4% for the PRGF group and 10% for the hyaluronan group. This difference was attributed exclusively to the treatment modality. However, these preliminary results need to be evaluated in randomized clinical trials.

Kon et al. used PRP intraarticular injections (3 PRP units of 5 ml each) to treat degenerative lesions of articular cartilage of the knee (5). One hundred consecutive patients, affected by a chronic degenerative condition of the knee, were treated with PRP intraarticular injections (115 knees treated). The preliminary results of this retrospective study suggest that the treatment was safe and had the potential to reduce pain and improve knee function and quality of life in younger patients with a low degree of articular degeneration.

Wang-Saegusa et al. used plasma rich in growth factors (PRGF) in patients with osteoarthritis of the knee (6). A total of 808 patients with knee pathology were treated with PRGF, 312 with osteoarthritis of the knee (Outerbridge grades I-IV) and symptoms of >3 months duration met the inclusion criteria and so were evaluated to obtain a sample of 261 patients, 109 women and 152 men, with an average age of 48.39. Three intraarticular injections of autologous PRGF were administered at 2-week intervals in outpatient surgery. At 6 months following intraarticular infiltration of PRGF in patients with osteoarthritis of the knee, improvements in function and quality of life were documented. The authors stated that these favourable findings indicate that PRGF could be considered as a therapy for osteoarthritis. However, the grade of evidence of Wang-Saegusa et al.'s study was low.

Filardo et al. investigated the favourable effects observed after PRP injections (7). The findings of their clinical retrospective study indicate that treatment with PRP injections can reduce pain and improve knee function and quality of life with short-term efficacy. However, the authors stated that further studies are needed to confirm these results and understand the mechanism of action, and to find other application modalities with different platelet and GF concentrations and injection timing, which would provide better and more durable results.

Dhollander et al.'s study focused on the treatment of patellar cartilage defects in the knee. Hence, he designed a study that described the technical details and presented the initial results of autologous matrix-induced chondrogenesis (AMIC) used with PRP gel, also known as the AMIC plus technique (8). They concluded that AMIC plus was feasible for the treatment of symptomatic patellar cartilage defects because there was a clinical improvement in all patients, although MRI findings did not confirm this positive outcome. However, the level of evidence of this pilot study was low (level IV) and included only five patients.

Dhillon et al. reported on the role of PRP intraarticular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis in a retrospective clinical study (9). Sampson et al. evaluated the clinical effects of intraarticular PRP injections in a small group of patients with primary and secondary osteoarthritis (10). In a study of 14 patients, patients with primary and secondary knee osteoarthritis received three PRP injections in the affected knee at 4-week intervals. The majority of the patients expressed a favourable outcome at 12 months after treatment. However, the study was uncontrolled, prospective and preliminary.

In a therapeutic case-control study with a grade III level of evidence, twenty five stem cell injections combined with arthroscopic debridement were administered to patients suffering from knee osteoarthritis (11). A mean of 1.89×10 stem cells were prepared with approximately 3.0 mL of PRP and injected in the selected knees of the patients (6). The mean Lysholm, Tegner activity scale, and VAS scores of the patients improved significantly by the last follow-up visit. Moreover, no major adverse events related to the injections were observed during the treatment and follow-up periods. The results were compared between the study and control groups, in which the patients had undergone arthroscopic debridement and PRP injection without stem cells. Although the preoperative mean Lysholm, Tegner activity scale and VAS scores of the study group were significantly poorer than those of the control group, the clinical results at the last follow-up visit were similar and not significantly different between the two groups. The short-term results of this study are encouraging and demonstrate that infrapatellar fat pad-derived MSC therapy with intraarticular injections is safe and helpful in reducing pain and improving function in patients with knee osteoarthritis.

Filardo et al. compared the safety and effectiveness of two PRP production methods, which were done as an intraarticular injection treatment for knee cartilage degenerative lesions and osteoarthritis (12). They studied 144 symptomatic patients with cartilage degenerative lesions and osteoarthritis (level of evidence II). Seventy-two patients were treated with 3 injections of platelet concentrate prepared with a single-spinning procedure (PRGF), the other 72 with 3 injections of PRP obtained with a double-spinning approach. The patients were evaluated prospectively at the enrolment and at 2, 6, and 12 month follow-ups with IKDC, EQ-VAS and Tegner scores; adverse events and patient satisfaction were recorded. PRP injections produced more pain and swelling reaction when compared to PRGF, PRGF, similar results were found at the follow-up periods, with a significant clinical improvement with respect to the basal level. Better results were achieved in younger patients with a low degree of cartilage degeneration.

Filardo et al. reported a randomized double blind prospective trial comparing PRP to hyaluronic acid injections for the treatment of knee chondropathy or osteoarthritis (13). Their results suggested that PRP injections offer a significant clinical improvement up to one year of follow-up. However, conversely to what was shown by the current literature, for middle-aged patients with moderate signs of osteoarthritis, PRP results were not better than those obtained with hyaluronic acid injections, and thus it should not be considered as a first line treatment. More promising results were shown for its use in low grade degeneration, but they still have to be confirmed.

Cerza et al. reported a randomized controlled trial, with a level 1 of evidence, indicating that treatment with 4 intra-articular injections of PRP showed a significantly better clinical outcome than did treatment with hyaluronic acid (14).

Gobbi et al. tried to determine the effectiveness of intra-articular PRP injections in active patients with knee osteoarthritis and to evaluate clinical outcomes in patients with

and without previous surgical treatment for cartilage lesions (15). The PRP treatment showed positive effects in patients with knee osteoarthritis. Operated and nonoperated patients showed significant improvement by means of pain reduction, and improved symptoms and quality of life. The clinical efficacy of PRP is still debatable and a standardized protocol has yet to be established.

In a randomized controlled trial, with a level 1 of evidence, Patel et al. treated 78 patients (156 knees) with bilateral osteoarthritis (16). Patients were divided randomly into 3 groups. Group A (52 knees) was administered a single PRP injection, group B (50 knees) was administered 2 PRP injections 3 weeks apart, and group C (46 knees) was administered a single normal saline injection.A single dose of WBC (white blood cells)-filtered PRP in concentrations of 10 times the normal amount was as effective as 2 injections to alleviate symptoms in early knee osteoarthritis. The results, however, deteriorated after 6 months. Both groups treated with PRP had better results than did the group injected with saline only.

Jang et al. analyzed the range of cartilage damage and patellofemoral joint degeneration in degenerative osteoarthritis and determined the duration for the positive effects of PRP injection (17). The study included 65 patients suffering from osteoarthritis that were treated with intra-articular PRP injection. Clinical improvement at 6 months post-procedure had been reported, but the symptoms tended to deteriorate one year after injection. While intra-articular PRP injection can be used for the treatment of early osteoarthritis, increasing age, and developing degeneration resulted in a decreased potential for PRP injection therapy.

Smelter and Hochberg reviewed new data on the pharmacologic treatment of osteoarthritis for the years 2011-2012 (18). Their main conclusion was that much research surrounding intra-articular injections of PRP has not produced clear evidence that this therapy is efficacious in osteoarthritis. Therefore, they concluded that at this time PRP requires more investigation.

Torrero et al. reported preliminary results of 30 patients affected by chondropathy of the knee after 6 months treated with a single intraarticular injection of PRP (19). Thirty patients with a diagnosis of I to III Outerbridge chondropathy in the knee were treated with one intraarticular injection of PRP. They found that one injection of PRP showed clinical improvement. However, they also stated that until the efficacy of PRP is not definitely demonstrated, orthopaedic surgeons should be very prudent in indications.

A one-year treatment of nine autologous PRP injections significantly reduced pain and improved quality of life in 51 patients with a low degree of femoro-tibial cartilage degeneration (chondromalatia grades II and III) (20). However, Magnetic Resonance Imaging (MRI) did not confirm any significant cartilage condition improvement. Some clinical studies in humans with a low grade of evidence, different scores to measure results (WOMAC, IKDC, VAS, Kellgren-Lawrence), different inclusion and exclusion criteria, and different osteoarthritis classification, suggest that PRP could have preventive effects against osteoarthritis progression. However, strong evidence from well-designed clinical trials to support PRP therapy for osteoarthritis of the knee joint is still insufficient. Moreover, is it nearly impossible to compare the results between the different studies reported between 2008 and 2013 (July) due to the aforementioned differences. Hence, there is no clear evidence that intraarticular injections of PRP are efficacious in osteoarthritis. Therefore, at this time PRP requires more investigation with better scientific studies performed to assess the efficacy of PRP with high powered randomized controlled trials using similar assessment tools.

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