Platelet-Rich Plasma (PRP) is a New Hope for Patients with Knee Joint Osteoarthritis

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Abstract

Background: Autologous Platelet-Rich Plasma (PRP) is the volume of plasma with a high platelet concentration above normal baseline values. Platelets are sources of high concentrations of cytokines and a group of growth factors which regulate healing processes as well as tissue regeneration. Osteoarthritis (OA) of knee is one of the most common debilitating conditions associated with pain and limitation in daily living activities which negatively affect quality-of-life. It is a disease of the entire joint, involving not only the joint lining but also cartilage, ligaments, and bone.

Aim of the Work: We aim to illustrate the role of Platelet-Rich Plasma in management of Osteoarthritis (OA) of knee.

Study Design: Narrative review article.

Conclusion: The current review revealed that Osteoarthritis (OA) of knee joint has multi mechanism and increase the risk of complications bed redden as such, accounts for burden on economics budget.

Keywords: Osteoarthritis - PRP – Cytokines-VAS score- Knee joint.

1. INTRODUCTION

Figure 1. Anatomy of knee joint
The anatomy of knee joint is very complicated as shown in (figure 1) so it is liable to trauma and OA. Osteoarthritis (OA) refers to a clinical syndrome of joint pain with multifactorial pathology that is characterized by the gradual loss of articular cartilage, osteophyte formation, sub-chondral bone remodeling, and inflammation of the joint (1).

It is a disease of the entire joint, involving not only the joint lining but also cartilage, ligaments, and bone.

It is characterized by breakdown of the cartilage, bony changes of the joints, deterioration of tendons and ligaments, and various degrees of inflammation of the synovium (2).

A recent cohort study concluded that radiologic features of knee osteoarthritis were very common in adults: 13% of women 45–65 years of age (an incidence of 3% per year). Osteoarthritis commonly affects middle age to elderly population.

Investigators have theorized the increase in osteoarthritis in women during menopause may partially be attributed to the hormonal factors (3) as shown in figure 2.

2. PATHOPHYSIOLOGY

In recent years, an increasing number of patients are being diagnosed with osteoarthritis, which has a notable impact on human health.

With aging of the population and increasing obesity, OA arises as a major public health problem and an important financial burden for the global economy. (4–6)

SO we can finally define osteoarthritis (OA) of knee as one of the most common debilitating conditions associated with pain and limitation in daily living activities which negatively affect quality-of-life. It is the most common form of joint disease and among the top 10 causes of disability worldwide. (10)

Diagnostic criteria for osteoarthritis have been developed by the American College of Rheumatology. These criteria are outlines in table 1.
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Table 1. Diagnostic criteria for osteoarthritis

| Grade | Description |
|-------|-------------|
| 1     | Doubtful narrowing of joint space and possible osteophyte lipping; |
| 2     | Definite osteophytes and possible narrowing of joint space; |
| 3     | Moderate multiple osteophytes, definite narrowing of joint space and some sclerosis and possible deformity of bone ends; and |
| 4     | Large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone ends (12-14). |

Figure 3. Pathological grads of knee OA

3. Treatment of Knee OA

The non pharmacological modalities include patient education, exercises and self management, lifestyle modifications such as dieting and weight reduction, walking supports (canes/crutches), bracing, shoe and insole modification, local hot/cold applications, acupuncture, and electromagnetic therapy. (15-16) Physical therapy is generally used, with exercises to maintain range of motion and strength. Pharmacologic therapies can be in the form of analgesics (paracetamol), NSAIDs, opioids, and slow-acting so-called nutraceuticals (glucosamine and chondroitin sulfate).
If orally administered drugs are ineffective (17). Intra-articular injections with corticosteroids seem to be safe. (18) More than one clinical guidelines reported high recommendations that these injections reduce pain for short term, especially if accompanied by effusion (19-20).

Glucosamine is one of the building blocks of cartilage, which can be taken as a tablet as a supplement to the diet, or sometimes as an injection (21).

The clinical guidelines of the American Academy of Orthopedic Surgeons reported strong recommendation of not prescribing glucosamine for symptomatic patients while other three guidelines (22) stated fairly low level strength of recommendation for conditional use or even uncertainty about it.

4. **Platelet Rich Plasma**

Autologous Platelet-Rich Plasma (PRP) is the volume of plasma with a high platelet concentration above normal baseline values (23). Platelets are sources of high concentrations of cytokines and a group of growth factors which regulate healing processes as well as tissue regeneration (24).

4.1. **Mechanism of Action of Platelet Rich Plasma**

Autologous platelet concentrate suspended in plasma, also known as PRP, can be prepared from samples of centrifuged autologous blood. Exposure to a solution of thrombin and calcium chloride degranulates platelets, results in the formation of platelet gel and this stimulate the release of growth factors and bioactive molecules (25).

Therefore, platelets actively participate in healing processes by delivering a broad spectrum of growth factors (insulin like growth factor, transforming growth factor b- I, platelet derived growth factor, and many others) and other active molecules (e.g., arachidonic acid metabolites, cytokines, chemokines, ascorbic acid, extracellular matrix proteins, and nucleotides) to the injured site (26).

These factors altogether contribute to comprehensive roles of PRP, including anti inflammation, angiogenesis, chondrogenesis, chondrocyte proliferation, bone remodeling, coagulation, and cell differentiation and this, in turn, reduces inflammation, pain & can then be used as an adjunct to surgery with the intent of promoting hemostasis and accelerating healing (27).

Use of platelet-rich plasma is considered experimental / investigational for all orthopedic indications. This includes, but is not limited to, use in the following situations:

A. Primary use (injection) for the following conditions (28-30):
   - Achilles tendinopathy,
   - Lateral epicondylitis,
   - Osteochondral lesions,
   - Osteoarthritis,
   - Plantar fasciitis

B. Adjunctive use in the following surgical procedures:
   - Anterior cruciate ligament reconstruction,
   - Hip fracture,
   - Long-bone nonunion
   - Patellar tendon repair,
   - Rotator cuff repair,
   - Spinal fusion

4.2. **Preparation of PRP**

The steps of preparation as shown in next figure; (4)
5. DISCUSSION

A number of RCTs and several systematic reviews of RCTs evaluating the use of PRP for knee osteoarthritis (OA) have been published. Protocols used in PRP interventions for knee OA varied widely (31). For example, in the studies identified in the Laudy et al (2015) systematic review, PRP was prepared using single, double, or triple spinning techniques and interventions included between 1 and 3 injections delivered 1 to 3 weeks apart. (32)

Xu et al (2017) conducted a systematic review and meta-analysis of RCTs comparing PRP with hyaluronic acid (8 trials), or placebo (2 trials), for the treatment of knee OA (see Table 1).21 Risk of bias was assessed using Cochrane criteria. Four studies were assessed as having low quality, three as moderate quality, and three as high quality. Meta-analyses including 7 of the trials comparing PRP with hyaluronic acid showed that PRP significantly improved Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) or International Knee Documentation Committee (IKDC) scores compared with HA at 6-month follow-up; however, when meta-analyses included only the 2 high-quality RCTs, there was not a significant difference between PRP and hyaluronic. (33-34) (Note that WOMAC evaluates 3 domains: pain, scored from 0-20; stiffness, scored from 0-8; and physical function, scored from 0-68. Higher scores represent greater pain and stiffness as well as worsened physical capability. The IKDC is a patient-reported, knee-specific outcome measure that measures pain and functional activity.) (35)

In the meta-analysis comparing PRP with placebo, a third trial was included, which had four treatment groups, two of which were PRP and placebo. This analysis showed that PRP significantly improved WOMAC or IKDC scores compared with placebo; however, only one of the trials was considered high quality and that trial only enrolled 30 patients. All meta-analyses showed high heterogeneity among trials (I2≥90%). (36)

Laudy et al (2015) conducted a systematic review of RCTs and nonrandomized clinical trials to evaluate the effect of PRP on patients with knee OA (see Table 1).14 Ten trials (total N=1110 patients) were selected. Cochrane criteria for risk of bias were used to assess study quality, with 1 trial rated as having a moderate risk of bias and the remaining 9 trials as high risk of bias. While meta-analyses showed that PRP was more effective than placebo or hyaluronic acid in reducing pain and improving function, larger randomized studies with lower risk of bias are needed to confirm these results. (37) Chang et al (2014) published a systematic review that included 5 RCTs, 3 quasi-randomized controlled studies, and 8 single-arm prospective series (total N=1543 patients) (see Table 1). (38) The Jadad scale was used to assess RCTs, and the Newcastle-Ottawa Scale was used to assess the other studies; however, results of the quality assessments were not reported. Meta-analysis of functional outcomes at 6 months found that the effectiveness of PRP (effect size, 1.5; 95% CI, 1.0 to 2.1) was greater than that of hyaluronic acid (effect size, 0.7; 95% CI, 0.6 to 0.9; when only RCTs were included). (39)

However, there was no significant difference at 12-month follow-up between PRP (effect size, 0.9; 95% CI, 0.5 to 1.3) and hyaluronic acid (effect size, 0.9; 95% CI, 0.5 to 1.2; when only RCTs were included). Fewer than 3 injections, single spinning, and lack of additional activators led to greater uncertainty in the treatment effects. PRP also had lower efficacy in patients with higher degrees of cartilage degeneration. Results were consistent when analyzing only RCTs, but asymmetry in funnel plots suggested significant publication bias. (40)

6. CONCLUSION

OA of knee joint is multi-factorial pathology and patients with OA of knee are really suffering.

IA injections of PRP and corticosteroids given together for knee OA are an effective non-operative modality of treatment. In combination, they seem to have better efficacy than any of them given alone. These injections are clinically safe and have promising and very positive effects for patient satisfaction.

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