Clinics in Surgery

Editorial
Published: 10 Nov, 2020

Platelet Rich Plasma as a Definitive Treatment Option in Articular and Musculoskeletal Diseases: Emerging Trend

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Editorial

Due to an improved understanding of the role played by growth factors in tissue healing and restoration, the use of Platelet Rich Plasma (PRP) has increased tremendously in the last couple of years. However its actual effectiveness is yet to be fully established. Several studies have demonstrated significantly better results with use of PRP in treatment of inflammatory and degenerative conditions; however, some authors have reported its utility as nothing more than a placebo. PRP is an autologous blood product, in which concentration of platelets are about 5 to 6 times higher than normal blood (baseline: 150-400 × 10^9 per L) [1]. Because of autogenous nature of PRP, the risk of immunogenicity and disease transmission related to grafts are negligible. In PRP, platelets release alpha and dense granules after activation by thrombin or calcium chloride. Various anti-coagulants are also used to prevent the early spontaneous activation of the platelets and platelet aggregation. The growth factors and cytokines released from these granules facilitate the process of cellular proliferation, chondrogenesis and angiogenesis [2]. In addition to growth factors it contains adhesion molecules that take part in bone formation. The active secretion of growth factors starts in 10 min after blood clotting and over 95% of the pre-synthesized growth factors contained in the granules are secreted within the first hour of PRP injection [3]. PRP is a potential orthobiologic agent and used in various musculoskeletal conditions. The first use of PRP was described by Marx in 1998 for repair of bony defects [4]. He reported good results in case series of mandibular continuity defects. But after that several studies showed contrary results and some other showed better results with use of PRP. Its use in some of important musculoskeletal conditions is explained as follows:

- **Osteonecrosis of femoral head (ONFH)**: During last thirty years, Core Decompression (CD) has been used in early stages of ONFH (Ficat I & II). But its cure rate is only 63.5% and efficacy remains doubtful. In order to improve the results of core decompression and also improve survivorship of hips in ONFH, PRP may be a useful adjuvant. In ONFH, PRP induces osteogenesis, angiogenesis by upregulation of PDGF, VEGF, IGF-1, TGF-β and inhibit inflammatory reaction by downregulation of IL-17A, IL-1β and TNF-α. A study by D'Ambrosi et al. [5] on treatment of ONFH (n=24 hips) in which CD combined with PRP, BmMSCs and synthetic bone graft were performed. They showed 80% hip survivorship in early stages of ONFH. Another study by Aggarwal et al. [6] (n=53 hips), in which they compared CD with or without use of PRP and followed up to 6 years. Hip survivorship in PRP group and non-PRP group was 92% and 78% respectively (p-value 0.01). So in early stages of ONFH use of PRP gives promising results and halts the progression of disease.

- **Knee osteoarthritis**: On an average, about 10% to 15% of people aged more than 60 years are suffering from Osteoarthritis (OA) of knee. In early stages of OA knee, use of PRP stimulates chondrocytes to produce cartilage matrix and down-regulates inflammatory mediators (IL-1). A systematic review by Fice et al. [7] on PRP use for cartilage pathology showed that PRP induces proliferation of chondrocytes, increases proteoglycan production, and leads to a greater deposition of type II collagen. In a meta-analysis by Shen et al. [8] on effect of PRP in OA knee patients (14 RCTs and 1423 patients) showed that PRP led to significant improvements in WOMAC scores at shorter follow-up at three- and six-months.

- **Nonunion of long bones:** Autologous cancellous bone is considered the gold standard for the treatment of non unions as a bone graft material. But due to donor-site morbidity and limited supply associated with it, there is always a need for better alternatives or adjuvants. Various growth factors and adhesion molecules in PRP induces cellular proliferation, matrix production, osteoid production and collagen synthesis. All these are required for fracture healing. Bielecki et al. [9] studied percutaneous injection of autologous platelet-rich gel in nonunion and delayed union. They

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Received Date: *05 Oct 2020*
Accepted Date: *04 Nov 2020*
Published Date: *10 Nov 2020*

Citation:
Aggarwal AK, Kumar K. Platelet Rich Plasma as a Definitive Treatment Option in Articular and Musculoskeletal Diseases: Emerging Trend. Clin Surg. 2020; 5: 2991.

concluded that union was achieved in all delayed union cases but in nonunion cases, union occurred only in 13/20 cases at an average of 10.3 weeks after injection. Another study on use of PRP injection reported fracture union in 82 out of 94 nonunion of long bone cases by the end of 4 months [10].

- **Tendon and ligament injuries:** Tendon and ligaments have poor vascular supply and heal slowly relative to other tissues. The role of PRP in rotator cuff tears and after repairs is to stimulate healing at the bone-tendon interface and also it decreases pain. In non-operative cases, PRP has been used as an alternative to steroid in subacromial impingement and partial tears, especially in high-level athletes. Shams et al. [11] conducted a RCT to compare corticosteroid and PRP injections in symptomatic partial rotator cuff tears. They reported that in PRP group, VAS and functional score improved at 12 weeks but there was no difference after 6 months.

- The effect of PRP use for Achilles tendinopathy treatment has also been investigated. In acute Achilles tendon injuries studies have shown a quicker recovery time and a better Achilles tendon rupture score but do not have effect on chronic or degenerative Achilles tendinopathy [12]. Similar results have been seen with patellar tendinopathy, acute hamstring injuries, lateral epicondylitis and ulnar collateral ligament tears. In these conditions PRP is used as a conservative treatment and it may decrease pain score in short term follow ups.

- **Intervertebral disc degeneration:** Intervertebral Disc Degeneration (IDD) is one of the major causes of low back pain. IDD is an active process. It involves changes in tissue and the cellular microenvironment that ultimately leads to structural breakdown and impairment of intervertebral disc function. In 2016, Levi et al. [13] demonstrated the effect of intradiscal PRP injection on discogenic back pain in 22 patients. After a 6-month follow-up period, 47% of patients reported at least a 50% improvement in pain and a 30% improvement in their Oswestry disability index score. Another study by Akeda et al. [14] also *proved the safety, feasibility and efficacy of PRP in the treatment of lumbar discogenic back pain.*

- **Prevention of blood loss in total knee arthroplasty:** Platelet rich plasma has been used to reduce blood loss in TKA. PRP releases thromboxane A2, thrombin, adenosine diphosphate and several growth factors which in turn attracts more platelets to the wound site. These large numbers of platelets form a platelet plug, augment the inflammatory cascade and result in hemostasis [15]. Aggarwal et al. [16] reported significant reduction in blood loss after the use of autologous platelet gel in patients of total knee arthroplasty.

- **Others:** In recent years PRP injections have been used for acute meniscal injuries, wrist pain of unknown cause and some other musculoskeletal conditions.

Conclusion

Several studies showed beneficial effect of PRP use as alternative treatment option. However, it is difficult to make a general conclusion on the use of PRP in musculoskeletal conditions. At the end, some more randomized clinical studies with more number of patients may require for better understanding of utility of PRP.

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