

## PRP in Orthopaedics- Where We Stand Today?

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The branch of regenerative medicine which deals with engineering, replacing or regenerating injured cells, tissues or organs is rapidly evolving in medicine to restore normal or near normal function & use of platelet rich plasma is one of its component especially in musculoskeletal problems. PRP is one of the extensively used 'Orthobiologic' agent. PRP emerged as the second generation of orthobiologics, and the first orthobiologic of the autologous form. The origin of PRP can be traced through the application of autologous blood products to facilitate healing. In recent years, Bone Marrow Concentrate (BMC) has emerged as the third generation of orthobiologic therapy. Its potent mixture of mesenchymal stem cells, hematopoietic cells, platelets and cytokines have been shown to possess anti-inflammatory, immunomodulatory and chondrogenic properties, which act as the foundation for its regenerative potential. The idea of using platelet rich plasma (PRP) in medicine has been around since the 1970s. It is only more recently that its use has been employed in the area of musculoskeletal science. The Platelet rich plasma (PRP) is an autologous blood-derived product that has an increased concentration of platelets that are rich in growth factors referred to as Autologous platelet concentrate (APC). It is created through a two-phase centrifugation process called plasmapheresis, in which liquid and solid components of anticoagulated blood are separated.

The first phase consists of an initial soft spin (1,200 to 1,500 RPM) with a relatively low gravitational force in which plasma and platelets are separated from red blood cells and white blood cells platelet-rich and platelet-poor plasma components. . A higher concentration or absolute number of platelets within PRP does not necessarily lead to an enhanced tissue healing effect. Literature suggests that the most efficacious platelet concentration for tissue healing is  $1.5 \times 10^6$  platelets per microliter. It has the potential to enhance the healing of tissue at the cellular level via the recruitment, proliferation, and differentiation of cells involved in tissue regeneration. In addition to platelets, PRP contains other cell types with potentially beneficial effects in tissue healing. More than 40 commercial systems exist that claim to concentrate whole blood into a platelet-rich substance. But fewer than five can remove >99% RBCs from the PRP sample. Now that the understanding of the cellular content of PRP has improved, newer generation PRP systems (with a more favourable formulation) are being created. When these are being used outcomes are more favourable.

Many successful studies have led to the official recognition of PRP use in orthopaedic societies and an increasing popularity in the field today. Some common diagnoses treated with PRP like Shoulder – Rotator cuff tendinitis or tear, rotator cuff impingement syndrome or bursitis, bicipital tendinitis, labrum tear, arthritis, instability; Elbow/Wrist/Hand – Tennis elbow, golfer's elbow, DeQuervain's Tenosynovitis, trigger finger, arthritis, other wrist or finger tendonitis; Hip – Iliotibial band tendinitis (ITB Syndrome), psoas tendinitis and bursitis, greater trochanteric bursitis, labrum tears, arthritis, sacroiliac joint dysfunction; Knee – Patellar tendinitis,

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partially torn or strained major ligaments of knee (ACL/LCL/MCL), meniscus tears, chondromalacia, arthritis, instability; Ankle – Achilles tendinitis, peroneal tendinitis, ankle sprain, instability, other foot or ankle tendinitis & Spine – Whiplash injury, ligament sprain, instability, rib problems, arthritis.

### Bone

Due to its osteogenic potential enhance bone grafting efficacy (both allograft and auto grafts) or be used to augment bone graft substitutes are attractive and PRP offers this potential as it contains a number of growth factors that can stimulate the proliferation and differentiation of cells of the osteogenic lineage. It has been also used in managing osteochondral dissecans (OCD) in association with micro fracturing of such lesions. PRP should be considered as a first line treatment of symptomatic osteochondral lesions of the talus. Presumably, it works through stimulating osteoblasts, fibroblasts, up regulation of osteocalcin and differentiation of mesenchymal stem cells into bone forming cells. Thus, it has been found to positively affect bone healing as well and successfully being tried in patients of non union.

### Tendon and Ligaments

Tendon and ligaments heal more slowly than most tissues due to poor vascular supply. This can result in new tendon tissue that does not have the same structural and functional properties as the original tissue when healed and leads to scar tissue. One possible explanation is that the poor blood supply results in a lack of adequate growth factors being delivered to the site of injury. Given, then, that there are problems with tendon and ligament healing, it is possible that PRP, as a good source of growth factors, may enhance healing. It has been found to re-initiate inflammatory phase, establishes balance between inflammatory & anti-inflammatory process, inhibit pain pathways, release of multiple growth factors to stimulate healing, stem cell migration & differentiation into tenocytes & fibroblasts. Use of PRP in Certain rotator cuff tears (including massive tears and chronic injuries), Achilles tendinopathy treatment & ankle sprains, Shoulder impingement syndrome has also been investigated. Use of PRP has also been explored in partial ACL tears and anterior cruciate ligament reconstruction (animal studies have been conducted using collagen-platelet scaffolds for supplementing ACL repairs have been found to be successful) & presently being successfully used in lateral epicondylitis and plantar fasciitis. Although the cost-effectiveness of treatment is unclear, the clinical evidence suggests that local injection of PRP containing WBCs may be beneficial to patients with chronic elbow epicondylitis refractory to standard nonsurgical treatment should be tried as confirmed by various studies.

### Muscle

As with the other tissues already discussed, it can be hypothesized that the use of PRP will accelerate muscle healing. PRP found to increase myocyte proliferation, up regulate expression of stem cell markers in human muscle derived progenitor cells, and increase early cell differentiation. At the current time, little evidence exists to support this association. Indeed, some researchers have suggested that PRP may actually lead to unwanted fibrotic healing in muscle & has also been shown to have nociceptive effects, when treated in acute muscle tears and also there has been significant reduction in the duration to return back to sport, when used in conjunction with surgical repair of muscle tears in sports athletes. It has been recommended to use ultrasound guided injection of PRP in the affected area.

### Cartilage

Articular cartilage lacks the vascularisation and inflammatory processes that enable effective repair. Endogenous chondrocytes can synthesize fibrous repair tissue but not sufficiently to fill even small defects with a cartilage-like matrix. PRP also has potential for particular cartilage repair by direct application into the damaged joint; either as a liquid gel or entrapped in a delivery device. Nevertheless it has been found to be beneficial in primary and secondary knee osteoarthritis. Here it has been found to improve lubrication in the joint by stimulating hyaluronic acid & lubricin production, stimulates cellular repair & reduces cartilage breakdown, helps in stem cell migration & differentiation & restabilizes an unstable joint.

### Meniscus

There are few studies specifically targeting menisci with PRP. Although menisci are not essential for joint function, meniscal resection leads to long-term destabilization and degradation of the articular surfaces. Autologous blood products such as PRP, Fibrin

and blood provide an increase of factors demonstrated to influence meniscal cells and may be one initial, simple, route to improve healing especially following meniscal surgery.

### Message

Orthobiologics, especially PRP, hold a lot of promise as upcoming and novel treatment modalities. PRP is a promising therapeutic agent for orthopaedic soft tissue injuries, but a better understanding of underlying biology & physiology of these pathologies will help identify appropriate clinical targets for PRP. For the clinician wishing to utilize PRP in practice, there are several important considerations that need to be made based on the conflicting meta-analyses for different conditions and the paucity of guidelines developed by professional organizations. However, PRP may provide some benefit in patients who have knee osteoarthritis and lateral epicondylitis. On the other hand, the evidence appears to be inconsistent or displaying a minimal benefit for PRP usage in rotator cuff repair, patellar and Achilles tendinopathies, hamstring injuries, ACL repair, and medial epicondylitis. PRP applications that are recognized by AAOS(American Academy of Orthopaedic Surgeons), AOSSM (American Orthopaedic Society for Sports Medicine), or ICMS (International Cellular Medicine Society) to have a positive effect Lateral Epicondylitis, Rotator Cuff Repair, Plantar Fasciitis, Osteoarthritis, ACL Repair, Achilles Tendinitis, Hamstring injury, Ankle sprains, Meniscal repair, Patellar tendinosis based upon multiple randomized controlled trials.

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