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Opinion

Clinical Applications of Platelet Rich Plasma in Musculoskeletal Disorders

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Platelet-rich plasma (PRP) therapy has been evaluated for its effect on acute and chronic tendinopathies, ligament rupture, acute fracture healing, bone non-union, muscle injuries, and degenerative joint disease. PRP initially was used in 1987 as a means of reducing homologous blood product transfusions during open heart surgeries and ever since autologous growth factors are used to enhance healing in indications such as oral and maxillofacial, plastic and reconstructive surgeries, cardiovascular medicine, ophthalmology, otolaryngology, and wound management.

The concept of using PRP to enhance local tissue healing is based on several growth factors. PRP therapy offers great potential and promise in treating musculoskeletal disorders. Platelets are frequently associated with haemostasis and in reparative role. Platelets carry storage organelles-known as granules (dense and α) which spill these contents on activation. The dense granules contain adenosine triphosphate, adenosine diphosphate, serotonin, and calcium which are primarily responsible for the coagulation cascade. The multiple cytokines and growth factors in response to platelet activation are released via exocytosis play a key role in wound healing process through 3 phases - inflammation, proliferation, and remodelling. The well-known growth factors in PRP to enhance local tissue healing includes Platelet-derived growth factor, Vascular endothelial growth factor, Transforming growth factor, Fibroblast growth factor, Epidermal growth factor, Hepatocyte growth factor and Insulin-like growth factor-1. The paracrine factors that are present in PRP stimulate angiogenesis to regenerate myocytes by enhancing the proliferation and migration of mesenchymal stem cells to the site of damage, cytokines and growth factors exert a heavy influence on the biology of their surroundings. Therefore, they may have a positive influence in clinical situations that require rapid healing and tissue regeneration. An ideal therapeutic PRP is considered to contain a platelet concentration of 3 to 4-fold increase to that of whole blood. It has been postulated that lower concentrations do not enhance tissue healing and that higher concentrations may be of no benefit [1,2].

PRP often prepared in orthopaedic clinics using a variety of point of care, closed-systems. Whole blood is obtained from the patient by venipuncture through a large-bore needle in order to prevent lysis and premature platelet activation. An alternative method of PRP graft preparation involves leukocyte-poor PRP. This is produced through a shorter single centrifugation process that concentrates platelets in a small volume of plasma while excluding the majority of WBCs. Once the platelet-rich product is obtained, it can be activated exogenously or endogenously to initiate degranulation and thereby release growth factors and cytokines. Exogenous platelet activation occurs ex-vivo and requires a platelet activator such as thrombin or calcium chloride to the PRP graft. Endogenous activation occurs in vivo and involves injecting the platelet-rich product directly into the target tissue and relying on contact with collagen or other biochemical mediators for clot formation and growth factor release. Once the platelet-rich plasma graft has been prepared, it is administered directly at the site of injury, usually through fluoroscopy, CT, or ultrasonography. If the graft is activated exogenously, the addition of thrombin or calcium chloride to the PRP results in polymerization of fibrin from fibrinogen, which creates a putty-like structure that can be placed directly into the region of injury or sutured at the surgical site.

PRP is considered to be safe treatment modality as it is autologous, with no concern of transmissible diseases or rejection-related issues (e.g. graft versus host disease) which are primarily seen with allogeneic transplants. Most of the commercially available PRP prepa-

ration kits are closed systems, the potential for contamination is limited. The risks associated with PRP include bleeding, deep organ puncture and infection. If bovine thrombin is used to activate the PRP exogenously before in vivo application, there is potential for allergic reaction. Activation with calcium chloride or endogenous thrombin eliminates that risk. The contraindications to PRP use is that most patients complaint of pain at site of injection which is due to acute inflammatory cascade response, PRP use is contraindicated in patients who have thrombocytopenia or a condition of platelet dysfunction.

Previous studies indicate that PRP therapy offers a great promise in musculoskeletal medicine. PRP therapy seems to show its greatest potential when used for chronic tendinopathy conditions, such as epicondylitis, chronic patellar and elbow tendinosis, chronic plantar fasciitis, rotator cuff. Several studies has showed a significant improvement in PRP treated groups compared to sham or corticosteroid injected groups. Several studies have shown promising results towards rotator cuff repair with standard surgical procedure. PRP has been well studied in the management of skeletal trauma, wherein the fracture hematoma, platelets aggregate and release growth factors. These human growth factors seem to stimulate the proliferation of human osteoblast-like cells. PRP has shown a rapid healing property in bone defects when treated along with bone graft. PRP has shown to be potential effective treatment for patients with osteoarthritis. Three injections of PRP in patients with osteoarthritic knees at 4-week intervals demonstrated a significant pain reduction with function resolution compared to baseline at 1 year post-treatment follow-up [3]. PRP has shown to reduce interleukin-1 β (IL-1β), a potent inflammatory factor in arthritis, in human osteoarthritic chondrocytes in vitro experiments [4]. Kon., *et al*. [5] showed significant objective and subjective improvements when injected PRP into 115 arthritic knees thrice at an interval of 21-days at 6 and 12-month post-treatment follow-up. Intra-articular injections of PRP in arthritic knees has shown significant clinical improvement compared to hyaluronic acid visco-supplementation [6].

To summarize PRP therapy has demonstrated to great potential for use in orthopaedic medicine in recent years with the ability to stimulate and enhance healing of soft tissue injuries. A caution must be taken in the use of platelet-rich plasma in only those clinical indications where there is anecdotal evidence available.

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