

# Platelet Rich Plasma in Focal Soft Tissue Rheumatism Including Spinal One

Md Abu Bakar Siddiq\*

Physical Medicine Centre, Chittagong, Bangladesh

\*Corresponding author: Md Abu Bakar Siddiq, MBBS, FCPS (Physical Medicine and Rehabilitation), Consultant, Physical Medicine Centre, Chittagong, Bangladesh, Tel: +8801718133427; E-mail: abusiddiq37@yahoo.com

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## Editorial

The first application of platelet-rich plasma (PRP) unveiled by Ferrari in 1987 as an autologous component after an open heart surgery [1]. Now there are at least five thousands registration in National Center for Biotechnology Information (NCBI) concerning PRP in various medical disciplines like orthopedic surgery, sports medicine, physical medicine, dentistry, neurosurgery, ophthalmology, urology, cosmetic, cardiothoracic surgery, etc. From the very launching period, platelet-rich plasma is being considered to be overwhelmingly promising and safe as well, enabling tissue healing through one's own natural growth factors [2]. It serves as a milieu of diverse biological mediators like insulin-like growth factor type I (IGF-I), transforming growth factor beta type 1 (TGF-1), platelet-derived growth factor (PDGF), hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), epithelial growth factor, and basic fibroblastic growth factors. Among them, IGF-I and HGF are plasmatic proteins and their concentrations are independent of platelet abundance. These growth factors along with cytokines/chemokines (Interleukin-8, IL-8; Macrophage inflammatory protein-1 alpha, MIP-1 $\alpha$ ; Epithelial Neutrophil-Activating Peptide 78, ENA-78; Monocyte chemotactic protein-3, MCP-3; Growth regulated oncogene-alpha, GRO alpha; angiopoietin-1, IGF-1 binding protein-3, etc.) and bioactive proteins (Von Willebrand factor, vWF; propeptide; Fibrinogen; Fibronectin; Vitronectin; Thrombospondin 1, TSP-1; laminin-8, alpha 4- and alpha 5- laminin subunits; signal peptide-CUB-EGF domain containing protein 1, SCUBE 1, etc.) are important in tissue repair and regeneration, wound healing, and even organ homeostasis [3].

As per definition, PRP should have higher platelet concentration; however, alongside following three factors we ought to take account while considering such formulation: 1) presence of leucocytes, 2) whether or not the PRP has been anti-coagulated, and 3) any requirement of exogenous activation. Graziani et al. suggested that the optimal platelet concentration in PRP should be 2.5 times more than that of baseline and quoted about detrimental outcomes if it houses more platelet than the aforementioned value [4]. Besides, platelet viability attributes to PRP quality, which largely depends on anti-coagulant used to prepare it. Among various anti-coagulants, FDA favors acid-citrate-dextrose combination for this purpose. White blood cells (WBC) especially neutrophils and macrophages also provide PRP with different biologic activities; though both are phagocytic and have potential of provoking tissue damage by releasing oxygen free radicals, macrophages can play offsetting roles between pro-inflammatory and anti-inflammatory aspects of tissue healing and their absence in PRP may affect tissue repair adversely [2]. Whether PRP should get activated or not before injecting is a topic of further debate. It can be activated exogenously using thrombin, calcium chloride or mechanical trauma, etc. If platelet-rich preparation has been activated in more

physiologic manner than too vigorously, a tetra-molecular stable, fibrin network will get formed, steeping up enmeshment of cells and growth factors. Prior to injection, PRP activation results in release of 90% preformed factors within minutes and as per literature review, *in vitro* activation of PRP is of paramount importance for surgical indications, though needless doing such while injecting soft tissue, rich with collagen, a potential natural PRP activator [3].

Being activated at injection site, platelet-rich growth factors are transformed into biologically active and bind with transmembrane receptors on target cells such as mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells, etc., thus initiating gene expression to direct tissue healing and tissue regeneration, with resultant formation of mature tissue, providing long-term stability [5]. After getting released, growth factors induce tissue healing following three distinct phases; inflammatory response (last about 3 days), proliferative phase (last several weeks), and tissue remodeling (last approximately 6 months) [6,7].

So far, effectiveness of platelet-rich formulation has been studied in various focal soft tissue rheumatism including nerve entrapment, muscle, tendons, ligaments, and fascial injuries, etc [5,8]. Even though most of the clinical evidences are of low-quality, they report overall good clinical outcomes following PRP intervention [9]. Usefulness of PRP in tendinopathy was first evaluated in early 1990s [9]. At that time physicians were more concerned about potential of prolotherapy in managing musculoskeletal disorders; nonetheless popularity of PRP increased since physicians began to witness substantial clinical recovery utilizing patients' own blood concentrate. The first clinical study focusing role of PRP in Achilles tendinopathy was performed by Filardo et al. in 2010 with good ultimate outcome [10]. Later on, similar result echoes in other clinical studies. However, the only randomized controlled trials available evaluating potential of a single PRP injection versus saline solution for the treatment of Achilles tendinopathy showed discouraging result; might be due to inappropriate PRP preparation, abysmal blood draw technique, or without prior PRP activation before injecting [11]. PRP also found to be efficacious in lateral epicondylitis, plantar fasciitis, partial rotator cuff tear, hamstring origin injury, jumper's knee, high ankle sprain, carpal tunnel syndrome, etc. [8,12-18]. Platelet concentrate also found to be profoundly beneficial while treating acute muscle injuries with faster recovery among professional athletes [18,19]. In their study, Raessadat et al. pointed out that both PRP and autologous whole blood injections were equally effective in treating lateral epicondylitis, but in long-term follow-up former one showed persistent efficacy in terms of pain relief and functional improvement [14]. In another study Yadav and colleagues compared the efficacy of PRP and methyl-prednisolone in lateral epicondylitis and they described PRP as a superior treatment option with sustained efficacy in this focal soft

tissue rheumatism [15]. Moreover, ultrasound-guided injection of platelet-rich concentrate seemed to be effective and safe in refractory rotator cuff tear [16,20]. Sheryp et al. first compared the utility of PRP and steroid injections in chronic plantar fasciitis both clinically and sonographically; albeit the cost of a platelet-rich preparation is higher than a steroid injection, former one can still be considered well-tolerated and appropriate choice for this common inferior heel suffering [17]. In an original work Mahindra and colleagues also described that, platelet-rich plasma was either equally or more effective than corticosteroid injection at 3 months of follow-up while managing chronic plantar fasciitis [21]. To be more, literature review documented 77.9% symptomatic improvement in plantar fasciitis at 1 year following PRP intervention [20]. In another systemic review by Franceschi et al., PRP intervention proved to be efficacious in managing plantar fasciopathy [13]. Similarly, Malahias et al. studied the result unmasked impressive effect of injection platelet-rich plasma in carpal tunnel syndrome; though recommended further evaluation with randomized controlled trial [8]. In a case report Peck and colleagues stated that PRP worked well in de Quervain's tenosynovitis if provided after ultrasound guided needle tenotomy [22]. Last but not least, it was Rowicki et al. who demonstrated the efficacy of platelet-rich plasma in managing pes anserine bursitis syndrome [23].

To sum up, effectiveness of intra-lesional steroid in managing non-infective focal soft tissue rheumatism is well-established particularly subjects refractory to conservative approaches [15,17]. However, recent time platelet-rich plasma is getting considered even more promising in dealing such clinical disorders with. Since PRP usefulness has been reportedly documented in some focal musculoskeletal disorders, we hope it will do well in others as well as for example, trigger fingers, trigger thumbs, bursitis, adhesive capsulitis, myofascial pain syndrome, etc.; henceforth recommend further clinical research. Lumbar ligamentous sprain, a regional soft tissue rheumatism, frequent in physiatrists', orthopedists' practice, reside over lumbar spine, common in athletes, report with history of preceding fall, weight lifting, etc. [24]; though responds well with intra-lesional steroid, contraindicates in some candidates. So, I surmise, platelet-rich plasma concentrate can be a justifiable option of treatment for this focal spine disorder as well in the ensuing days.

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