Editorial

Platelet-rich plasma therapy: A novel application in regenerative medicine

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Plasma samples with platelet concentration above base line values are referred to as platelet-rich plasma (PRP).[1,2] The clinical efficacy of the PRP was discovered in early 1990s when new "biological glues" were being discovered. They are at present being extensively used in many clinical and surgical fields requiring tissue regeneration such as orthopedics, dentistry, wound healing, and maxillofacial surgeries.[3] The therapeutic effect of PRP is attributed to the abundance of various growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β, fibroblast growth factor, insulin-like growth factor-1 (IGF-1), IGF-2, vascular endothelial growth factor, epidermal growth factor, and also some cytokines[4] primarily stored in alpha granules.

PRP can be classified into pure – platelet rich plasma (P-PRP), leucocyte and platelet rich plasma (L-PRP), pure platelet rich fibrin (P-PRF), leucocyte and platelet rich fibrin (L-PRF) based upon the technique used to prepare and the final content of the product.[5] Serum eye drops and PRP eye drops are also available these days for ophthalmic use.[6] PRF has been reported to be better than traditional PRP because it simulates the physiological process of platelet degranulation releasing varied growth factors.[5,7] Studies have also shown that leukocyte poor product is superior compared to leukocyte rich product as residual leukocytes can produce localized inflammation.[8]

PRP can be prepared either from autologous or allogenic source. Majority of studies documented have used autologous platelets preparations as they are more acceptable to the patient and carry lower risk of transmission of viral infections.[6] The PRP is usually prepared by centrifugation of whole blood collected in a sterile container using citrate-based anticoagulant. The centrifugation can be a one-step or two-step protocol. After final centrifugation, a platelet pellet is formed which is resuspended in a small volume of platelet-poor plasma. Further, the platelets in PRP are usually activated by addition of various activators (calcium chloride, thrombin, chitosan, and batroxobin) for release of growth factors.[9] Centrifugation and activation methods are the two important modifiers which have a critical impact on the quality of PRP and release of growth factors. Different studies have used different centrifugation conditions and there is no universally accepted protocol till date. Commercial PRP preparation systems are also available nowadays. These systems consist of desktop centrifuge and single use blood collection tube kits. Availability of such systems has led to the unregulated preparation of the autologous PRP in small laboratories outside the blood bank setup. These laboratories have minimal knowledge as well as training of process control and good manufacturing practices in handling this blood-derived material.

This issue of Asian Journal of Transfusion Science includes two articles on clinical efficacy of the use of PRP. The authors have used different methodologies and source for PRP preparation. Singh *et al.*[10] have shown the beneficial effect of autologous PRP in treatment of androgenic alopecia. They observed that by the end of 12 weeks all the 10 patients included in the study had good hair growth. They concluded that beneficial effects of PRP may be attributed to PDGFs influencing the function of hair follicles ultimately resulting in improved hair growth. On the other hand, Sonker *et al.*[11] have evaluated the role of platelet growth factors from allogenic ABO-matched PRP for clinical improvement in split thickness skin graft. They observed that there was 100% uptake of the graft in the wound area where PRP was applied.

Regulatory Issues

PRP is a biological product.[12] The biological product and the device used for its preparation should fall under the purview of regulatory authorities. In India, for preparation of both "plasma" and "platelets," blood banks need to obtain licence

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from Central Licence Approving Authority. However, the Drug and Cosmetics Act, 1940, is silent about the preparation, quality control, and use of PRP in regenerative medicine. In USA also, there is a lot of confusion with regard to regulatory issues of autologous PRP preparation device and its final product. All the PRP preparation systems in USA are brought to the market via 510 (k) clearance which certifies that the safety and performance of the device is substantially equivalent to a predicate PRP device. Nevertheless, here the device is controlled but not the final PRP product.[13] It is of concern as the final content of the product depends upon the device used.

Challenges and Future Directions

PRP preparations are being extensively used in wound healing and tissue repair despite of insufficient evidence support.[14,15] Blinded, multicentric, randomized controlled studies with large sample sizes to establish their therapeutic efficacy is the need of hour. There are no universally established standards for collection, quality control, and administration of the product.[15] In addition, the threshold dose required for therapeutic benefit is also undefined for different clinical indications. Hence, guidelines for the same need to be laid down by regulatory authorities to ensure its rational use. Although no adverse effects have been reported till date, patient safety still remains a major concern. All this emphasizes the role of transfusion medicine specialty in assuring quality, consistency, and safety of the product.

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