Platelet-rich Plasma by Single-spin Process in Male Pattern Androgenetic Alopecia: Is it an Effective Treatment?

This commentary is about the article on “Platelet-rich plasma by single-spin process in male pattern androgenetic alopecia: Is it an effective treatment?”

The inception of the therapeutic use of autologous platelets came from the local benefits of platelet-derived growth factor (PDGF) on wound healing and tissue repair. Since then, platelet-rich plasma (PRP) has seen an exponential rise in the number of indications in various fields of medicine. Also, PRP is seemingly housing its place in the field of dermatology, especially hair restoration. In an earlier article, I have illustrated the molecular effector pathways upregulated by the various growth factors that can potentially reverse the miniaturization in androgenetic alopecia (AGA).

As the name suggests, PRP is the volume of autologous plasma having platelet concentration above baseline (average 200,000 platelets/μL). Eventually, plasma fraction with any platelet concentration above $2 \times 10^5\ \text{μL}^{-1}$ is being referred to as PRP, which is potentially dissimilar and rather portends an overgeneralization of the term. In the last few years, various manual, semiautomatic, and fully automated commercial systems have become available, but each technique leads to different concentrations with dissimilar biology. There is evidence to suggest that the content of growth factors hugely varies, depending on the method of preparation of PRP.

Hence, it is very important to approach PRP in a rational way. The scientific proof of bone and soft tissue healing enhancement has been shown using PRP with 1,000,000 platelets/μL; henceforth, Marx in 2001 had recommended this concentration of platelets in a 5-ml volume of plasma, as the working definition of PRP. Investigational studies are long awaited to standardize the growth factor concentrations suitable for hair regrowth. Until then, we must adopt the above definition for PRP and should not incorporate all concentrations of PRP prepared by different methods, under the umbrella term PRP, which per se sends a very wrong message to the readers. Furthermore, extreme caution must be exercised while interpreting clinical studies utilizing PRP.

The authors have reviewed the clinical trials on this subject, and all of the discussed studies have reported positive results as against the negative results in their own study with PRP therapy. On analyzing, they have rightly found the double-spin method and the higher platelet concentrations in all studies, as against their own single-spin method of PRP preparation. Systematic reviews from the available literature have also pointed out discrepancy in results, which is partly because most of the studies are not controlled trials. But this might majorly relate to the wide heterogeneity of the product in use.

The American Association of Blood Banks technical manual states that “PRP is separated from whole blood first by ‘soft-spin’ centrifugation and then the platelets are concentrated by ‘hard-spin’ centrifugation with removal of the supernatant plasma.” The double-spin method is preferred over the earlier prevalent single-spin method as the desired concentration of platelets was not achieved by the latter. Also, to achieve the same, more amount of blood has to be withdrawn. Dhurat et al. have shown that a 30 ml venous blood yields approximately 3–5 ml of desired PRP depending on the baseline platelet count of an individual.

Studies have shown that clinical efficacy can be expected with a minimum increase of 4–6-fold from the baseline (i.e., ≥1 million platelets/μL). In principle, from the clinical point of view also, a dose–response relationship over cell proliferation is expected. Further, a bell-shaped response curve indicating a dose-dependent nature has been shown to be associated with PRP. Giusti et al. demonstrated that lower or higher concentrations than 1.5 million platelets/L, seemed to inhibit the angiogenic potential in human endothelial cells. In vitro studies on dermal papilla cells have also supported PRP at concentrations of 5–10 times the mean levels.

Ehrenfest et al. had categorized PRP into types, namely leucocyte-rich PRP (L-PRP), pure-PRP (P-PRP), leucocyte-rich platelet-rich fibrin (L-PRF), and pure platelet-rich fibrin (P-PRF); out of which L-PRP is most commonly prepared by the manual method for AGA. L-PRP, classically prepared by the Platelet Concentrate Collection System (PCCS; 3i/Implant Innovations, Palm Beach Gardens, FL) differs significantly from the P-PRP, as prepared by Anitua’s plasma-rich-in-growth-factors (PRGF kit; G.A.C. Medicale San Antonio, Vitoria, Spain). L-PRP is leucocyte-rich, which also has significantly higher concentration of platelets as well as growth factors [tumor growth factor (TGF)-β1 and PDGF-αβ]. This arises because of the overlapping specific gravities of the different cell types, and hence, L-PRP is able to harvest the near complete amount of platelets. Use of L-PRP has been evaluated in a study on AGA by Schiavonne et al. in which it led to an increase in hair thickness and numbers compared to baseline, resulting in a clinically important difference in over 40% of patients.

Further, in L-PRP, the platelet as well as the “bioavailable” growth factor concentrations differ according to the
device employed to prepare L-PRP. To date, there is no information on the influence of different preanalytical sample preparation methods on the detectable amount of growth factors.\[^{17}\] Unfortunately, these parameters have not been standardized.

Mazucco et al.\[^{18}\] have compared PRP prepared by three different legally marketed commercial devices, namely RegenPRP-Kit\(\textregistered\); Fibrinet\(\textregistered\); Plateltex\(\textregistered\) and one manual method customized at their blood transfusion center. PRP was prepared by differential centrifugation parameters in accordance with the instructions provided by each manufacturer, in which single spin was carried out only for RegenPRP, while rest of the three utilized double-spin method. The final mean platelet concentration (× times that of whole blood) was: Fibrinet 1,358 ± 419 × 10\(^3\) μl\(^{-1}\) (3.9×), Regen 430 ± 109 × 10\(^3\) μl\(^{-1}\) (1.6×), manual method 1,196 ± 188 × 10\(^3\) μl\(^{-1}\) (4.4×), and Plateltex 1,160 ± 164 × 10\(^3\) μl\(^{-1}\) (4.4×). This clearly shows that L-PRP prepared by double-spin process produced the desired “therapeutic” platelet concentration, as against the single-spin process. Interindividual variability was evidenced with the high standard deviation values. On comparing the mean concentrations of growth factors also, PRP obtained with manual double-spin method had nearly 4–5 times (within the therapeutic range) more concentration of PDGF-ββ, β-fibroblast growth factor, vascular endothelial growth factor, and TGF-β than that prepared by single-spin process for RegenPRP.\[^{19}\] At present, there are only isolated reports of clinical trials of PRP treatment in AGA with single- and double-spin methods, but clinical studies on comparative efficacy of the two would be welcome. Literature has suggested that low concentration PRP, i.e., lower than 1,000,000 platelets/μl, is associated with resultant negative clinical response.\[^{19}\] In a double-blind placebo-controlled pilot study on 26 women with AGA, Puig et al.\[^{19}\] showed no significant improvement in hair count or hair mass index with PRP. They had utilized Angel PRP system, which prepared low concentration, leucocyte- and erythrocyte-free PRP with approximately 2.75 to 3.4× platelet concentration. On the contrary, positive results have occasionally been shown by similar concentrations, but primarily in anecdotal reports.\[^{20}\] Interestingly, Gkini et al.\[^{21}\] have reported successful outcomes even with single-spin method PRP, and moreover, by the same kit (RegenKit BCT-3) as also used by the authors in the preceding study. However, not going by the manufacturer’s protocol, they reconcentrated the plasma separated after single spin, by manual removal of some amount of PPP, by virtue of which they achieved 5.8× platelet concentration.\[^{21}\] Hence, one can easily presume the improved platelet concentration, though with the same preparation device, accountable for the positive response in this study.

The reproducibility of the PRP preparation kits is another matter of concern. While the resulting platelet concentration can still be slightly manipulated by adjusting the total volume of the final concentrate, the platelet collection or harvesting efficiency tends to differ significantly between kits. For example, the Smart PReP\(\textreg\) system (Harvest Technologies Corporation, Munich, Germany) has a significantly \((P < 0.001)\) higher collection efficiency (63.4 ± 7.9%) than the Friadent-Schütze kit (PRP kit; Friadent-Schütze, Vienna, Austria) (49.6 ± 13.6%).\[^{22}\]

Hence, a prudent clinician must also check for the platelet collection efficiency of a particular device, before opting for one.

To conclude, numerous preparation devices are available, each with a peculiar technical characteristic (disparity of tubes, centrifugation force, separator gels), cumulatively affecting the amount and the kinetics of the release of growth factors, but their clinical significance and therapeutic implication in various indications of dermatology is yet to be ascertained. However, all the arbitrary target of platelet concentration of ≥1 × 10\(^3\) platelets per ml, i.e., 4–7-fold platelet concentration in whole blood, prevails for therapeutic application in the field of hair restoration. To prepare the same, a minimum of 25–30 ml of venous blood needs to be withdrawn. For a practicing trichologist, one must always check for the platelet concentration on each patient at every particular treatment session. On a related note, a global consensus is needed on terminology of PRP, particularly for standardizing clinical trials. At the same time, commercial interests should not tend to cause an eclipse of the true clinical benefits of PRP, which is a promising novel therapeutic modality in AGA.

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