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Case Report



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Injectable-Platelet-Rich Fibrin-Smart Blood with Stem Cells for the Treatment of Alopecia: A Report of Three Patients

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ABSTRACT

Hair loss or alopecia in males is very common, and so is its treatment. Until now, platelet-rich plasma has been in use for hair regeneration, which has shown results but lacks regenerative potential as compared to platelet-rich fibrin (PRF). Injectable-PRF (i-PRF) is advanced version of PRF in liquid form which can be injected and contains stem cells with high regenerative potential. Hair regeneration in Type VI and Type VII was observed which are difficult to treat. Hair growth with i-PRF has better regenerative potential. All cases reported showed improvement in hair growth.

Key words: Alopecia, growth factors, injectable-platelet-rich fibrin, regeneration, stem cells

INTRODUCTION

In every few years, there happen few inventions or discoveries in the field of dentistry which change its face for the larger benefit of people. Second-generation platelet concentrates also known as platelet-rich fibrin (PRF) is one such discovery by Dr. Choukroun which not only has applications in the mouth for bone augmentation but also can be used anywhere to enhance wound healing and re-establish angiogenesis.

PRF is actually a new platelet concentrate concept^[1] which accumulates platelets and the released cytokines in a fibrin clot.^[2] Advanced-PRFTM (A-PRFTM) and injectable-PRF (i-PRF), on the other hand, are different from conventional PRF and is based on the concept that low speed of centrifugation, yields maximum results and significantly higher number of leukocytes, platelets, and growth factor concentration-enhancing the regeneration process. Based on this PRF, like platelet-rich plasma (PRP) has wide applications in the field of oral and maxillofacial surgery, periodontology, orthopedics, dermatology, plastic surgery, burn wounds, diabetic foot, and wherever regeneration is required.

Various conditions can cause hair loss, and out of various types, androgenic alopecia (AGA), by far is the most

common type characterized by progressive hair loss caused by androgenic miniaturization of the hair follicle (HF), and has a gradual increase in incidence by age.^[3] Alopecia is difficult to treat especially at advanced stages such as Norwood-Hamilton Type VI and VII cases. However, certain drugs, hair transplant therapy, and injection of PRP help in hair growth.^[4] PRP has shown great success in the treatment of hair loss. Growth factors secreted by activated platelets in PRP help in hair growth. However as aforementioned PRF is an advanced version of PRP, thus authors decided to use i-PRF instead of PRP for treatment of AGA.

MATERIALS AND METHODS

Here, authors have discussed three cases with a varying degree of hair loss in patients between 35 and 40 years of

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age. Patients reported for the first time to the dental clinic with primary complaint of tooth pain. However, patients were counseled regarding the useful effects of PRF, and they all agreed to undergo the therapy. According to the Norwood–Hamilton classification Case 1 was classified as Type I [Figure 1a], there was no recession of the hairline, Case 2 [Figure 2a] can be classified as Type VI and Case 3 [Figure 3a] as Type VII.

In all the three cases shown here, in two 10 ml i-PRF tubes, 20 ml of blood was collected and centrifuged at 700 rpm for 4 min using A Duo centrifuge (Process for PRF, Nice, France) [Figure 4]. i-PRF liquid was collected using 31G insulin syringes (4 mm) and was injected through a hypodermic needle entering for 2–4 mm of the scalp. Along with the injections, the microneedling was done with a Dermapen. The whole procedure was completed in <10 min. Patients underwent for four sittings at a gap of 15 days each following the Cleopatra technique™. A-PRF was not used in the process. Postoperatively, patients were asked not to wash their head for 8 h, and to avoid exposure to sun or dust, or cover their head and restrict activities like swimming for 1 week at least.

No medication was prescribed except for pain control tablet diclofenac 50 mg si opus sit (SOS). On follow-up visits, it was learnt that patients did not have any postsurgical pain and any medication for pain was not required.

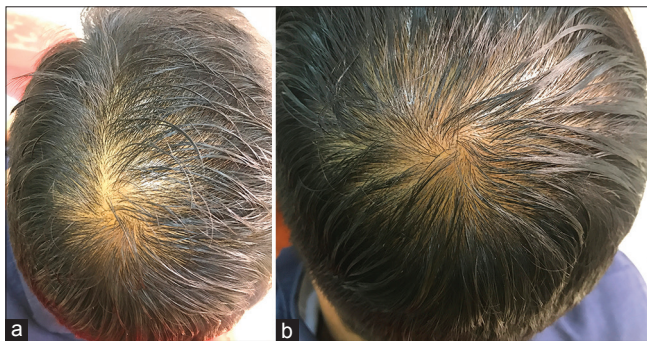


Figure 1: (a) Preoperative. (b) Postoperative after 4 sessions

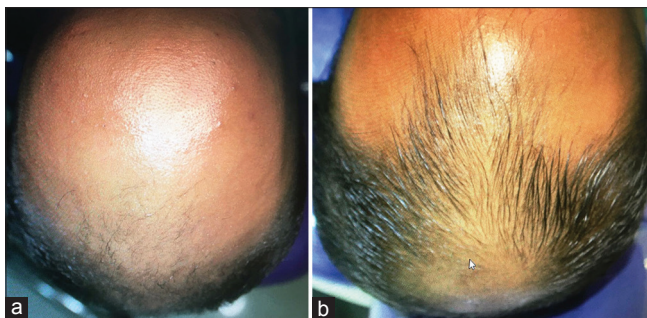


Figure 3: (a) Preoperative. (b) Postoperative after 4 sessions

RESULTS

Postoperatively, there was mild bruising and inflammation of the scalp which lasted for 2–3 days. There was no pain and any medication to control pain was not required. In Case 1, [Figure 1a and b] after four sessions of i-PRF therapy, the patient was satisfied with the amount of hair growth and did not want further sessions. The same was observed in Case 2 [Figure 2a and b]. However in Case 3 [Figure 3a and b], which is usually difficult, to treat, a slight amount of hair growth could be noticed by the patient and was willing to take further sessions of i-PRF. The results were based on the clinical outcomes and subjective questionnaire based on the patient's satisfaction, concluding in no further treatment.

DISCUSSION

AGA, as discussed earlier, is the most common type of hair loss and occurs due to two prime reasons genetic predisposition and hormonal stimulation.^[4] There are various treatment options available to treat AGA, such

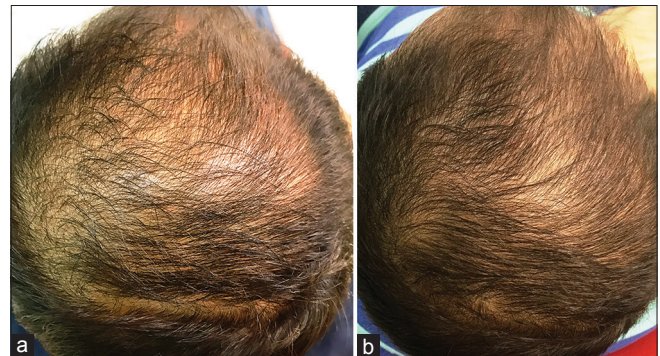


Figure 2: (a) Preoperative. (b) Postoperative after 4 sessions



Figure 4: Procurement of injectable-platelet-rich fibrin

as, hair transplant, medications such as finasteride and minoxidil with low-level laser light therapy, Stimulant and anabolic substances such as creatine, weight gainers, arginine and ornithine, growth hormone, somatomedin-C analogs, fat burners, whey protein isolate, branched-chain amino acids, steroids, and pro-hormones and PRP.^[4] All the treatment modalities offer little help except PRP which improves hair growth by constant supply of various growth factors. However, there is an ever-increasing need for better treatment protocols which can provide patients' satisfaction and redeem his/her self-esteem.

Most studies^[5-7] using PRP for hair growth have shown excellent results, and hence, the question arises is that why to use PRF when PRP has been in use. Marwah *et al.*^[8] stated that PRP provides 300%–700% enrichment of platelets. However, its optimal concentration is still unclear. Authors also stated that though the method of procurement is not similar, PRP has shown promising results in various fields and conducted a pilot study of treatment with weekly PRP for six sessions on ten patients with AGA Grade II or III and reported improvement in two patients only, raising questions like when to inject PRP? Moreover time frame of the procedure required? And concluded that PRP can only be used as an adjuvant for the treatment of hair loss and should not play a lead role. With PRF, may be, such questions can be answered.

Masuki *et al.*^[9] stated that A-PRF has a high concentration of white blood cells (WBCs) and platelets, whereas in PRP inflammatory cytokines were not present in high levels and there was no positive correlation between WBC counts and pro-inflammatory cytokine observed. Based on their study, authors concluded that A-PRF contains a higher amount of growth factors as compared to PRP, which not only functions as a scaffold but also a reservoir of growth factors.

Both PRP and PRF are platelet concentrates and PRP's role in the healing of hard and soft tissue has been well established; however, double centrifugation process, the addition of anticoagulants and bovine serum limits PRP's clinical application which calls for alternative, clinically feasible strategies.^[10] PRF is one such platelet concentrate which requires one spin and does not use anticoagulants for its procurement.^[1] According to the authors, PRF was developed with the idea of keeping methodology convenient and applicable for clinical use.^[1,2] Its three-dimensional fibrin network mimics the extracellular matrix in terms of its structure,^[11,12] which creates the environment for cells to function optimally.

In 2003 Gordon^[13] first proposed the concept that macrophages are involved in tissue healing. Authors reported that macrophages are an important source of interleukin-10 (IL-10) which inhibits pro-inflammatory cytokine production. In the experiment conducted, IL-10 deficient mice develop widespread inflammatory cell infiltrates, suffered septic shock and overactivity of pro-inflammatory cytokines, making authors to state that macrophages are involved in fibroblast recruitment, in the growth of new blood vessels making the site highly vascular creating growth and connective tissue remodeling. Recent research has shown that neutrophilic granulocytes not only play an important role in the early inflammatory process but also have tissue regeneration properties.^[10] They facilitate phagocytosis of necrotic and apoptotic cells via monocytes^[14,15] and wound debridement by secreting several proteases.^[14,16]

Choukroun and Ghanaati^[17] in their experimental study showed that low speed of centrifugation, just enough to separate platelets from red blood cells yields maximum results and a significantly higher number of leukocytes, platelets, and increase in growth factor concentration as compared to conventional PRF protocol. This new protocol also resulted in the generation of an injectable liquid PRF matrix (i-PRF) without the use of anticoagulants. Authors also claim that i-PRF prepared according to the low-speed centrifugation concept is highly enriched with platelets, leukocytes and provides an increased concentration of growth factors (vascular endothelial growth factor [VEGF] and transforming growth factor- β 1) which are very much required for neovascularization and angiogenesis. A-PRFTM and i-PRF contain monocytes which play an essential role on bone growth, vascularization, and production of VEGF. The monocytes have BMP receptors and produce BMP-2.^[18]

Thus, Choukroun's i-PRF derived from human blood contains a variety of blood cells including platelets, B- and T-lymphocytes, monocytes, stem cells, and neutrophilic granulocytes as well as growth factors.^[10] Experimental studies demonstrated that even dermal prekeratinocytes, human gingival fibroblasts, preadipocytes, and maxillofacial osteoblasts underwent differentiation and proliferated with Choukroun's PRF.^[10]

The results of i-PRF can be very well appreciated from the cases shown by the authors. Advanced alopecia where balding is severe becomes difficult to treat. In the cases shown, it can be easily stated that severe balding can be treated, not as an adjunct therapy but as the main treatment protocol without any prescription of medication.

According to Cleopatra technique™, 4 sittings are required at a gap of 15 days each; however in authors' opinion, session can be extended up to 6–7 times, till the patient is not satisfied.

CONCLUSION

There are reports of successful hair growth by PRP treatment protocol. However as the literature suggests i-PRF has benefits over PRP which can be utilized wherever growth and regeneration is required. As aforementioned, all cases showed improvement in hair growth. The sessions can be extended to get better results. Hair regeneration with i-PRF is relatively new with no changes in methodology involved with the use of PRP; however, larger sample size, longer duration of the patient follow-up and a control group is further required to study the effects of i-PRF on hair regeneration.

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Conflicts of interest

There are no conflicts of interest.

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