

Review  
Article

# Platelet-rich plasma in dermatology: Boon or a bane?

Arshdeep, M. Sendhil Kumaran

Department of Dermatology,  
Venereology and Leprology,  
Postgraduate Institute of  
Medical Education and  
Research, Chandigarh, India

**Address for correspondence:**

Dr. M. Sendhil Kumaran,  
Department of Dermatology,  
Venereology, and Leprology,  
Postgraduate Institute of Medical  
Education and Research,  
Chandigarh - 160 012, India.  
E-mail: drsen\_2000@yahoo.com

## ABSTRACT

There has been a recent spurt in application of platelet-rich plasma (PRP) in dermatology and aesthetic medicine. However, the details regarding use of PRP in various dermatological indications ranging from hair restoration to chronic ulcers are dispersed in literature, herein we have tried to focus all under one heading. Overall, PRP seems to be a promising therapeutic modality but the level of evidence as of now, from the available published data is low. This review will also stimulate readers to carry out well designed, larger population based trials, so as to validate its use in dermatology practice.

**Key words:** Androgenetic alopecia, platelet-rich plasma, rejuvenation, ulcers

## INTRODUCTION

Platelet-rich plasma (PRP) (*syn.* autologous platelet gel, plasma-rich growth factors and platelet-concentrated plasma) means “abundant platelets that are concentrated into a small volume of plasma.”<sup>[1]</sup> The pivotal discovery of platelet-derived growth factor (PDGF) in promoting wound healing, angiogenesis and tissue remodelling threw light on this novel autologous therapeutic modality. The documented success of PRP in dentistry and surgery as shown by Marx and co-workers,<sup>[1]</sup> have fuelled research on its role in other specialities like dermatology and aesthetics.<sup>[2]</sup> Takakura *et al.*,<sup>[3]</sup> revealed that PDGF signals in cell interactions are required for hair canal formation and growth of dermal mesenchyme, thereby opening newer perspectives for PRP in hair restoration.<sup>[3]</sup> Data regarding application of PRP in dermatology and aesthetics is dispersed in literature, hence in this write-up we have tried to focus all under one heading, which will provide the reader a comprehensive information regarding PRP.

## WHAT IS PRP?

PRP is an effective concentration of multiple fundamental growth factors (GFs) by virtue of platelets alone (stored as  $\alpha$ -granules in platelets) as enumerated in Table 1 and plasma proteins, namely fibrin, fibronectin and vitronectin. This cocktail of GFs is pivotal in modulation of tissue repair and regeneration,<sup>[4]</sup> whereas the plasma proteins act as a scaffold for the bone, connective tissue and epithelial migration.

Degranulation of the pre-packaged GFs in platelets occurs upon “activation” i.e., on coming in contact with coagulation triggers. The secreted GFs in turn bind to their respective transmembrane receptors expressed over adult mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells.<sup>[5]</sup> This further induces an internal signal-transduction pathway, unlocking the expression of a normal gene sequence of a cell like cellular proliferation, matrix formation, osteoid production, collagen synthesis, etc., thereby augmenting the natural wound-healing process.<sup>[6]</sup>

## PREPARATION OF “ACTIVATED PRP”

PRP is prepared either manually or by the use of automated devices, in a day care setting just prior to the procedure. The process must be carried out under strict aseptic conditions as well as optimum temperature regulations i.e., 20-22°C. In order to

Access this article online	
Quick Response Code:	Website: <a href="http://www.ijdv.com">www.ijdv.com</a>
	DOI: 10.4103/0378-6323.125467

**How to cite this article:** Arshdeep, Kumaran MS. Platelet-rich plasma in dermatology: Boon or a bane?. Indian J Dermatol Venereol Leprol 2014;80:5-14.

**Received:** May, 2013. **Accepted:** August, 2013. **Source of Support:** Nil. **Conflict of Interest:** None declared.

inhibit platelet aggregation, it is prepared with an anticoagulant, commonly using anticoagulant citrate dextrose solution formula A (ACD-A) or sodium citrate. The platelets need to be sequestered in high concentrations, enough for achieving therapeutic benefit and in a viable state at the same time, so that they can actively secrete their GFs.

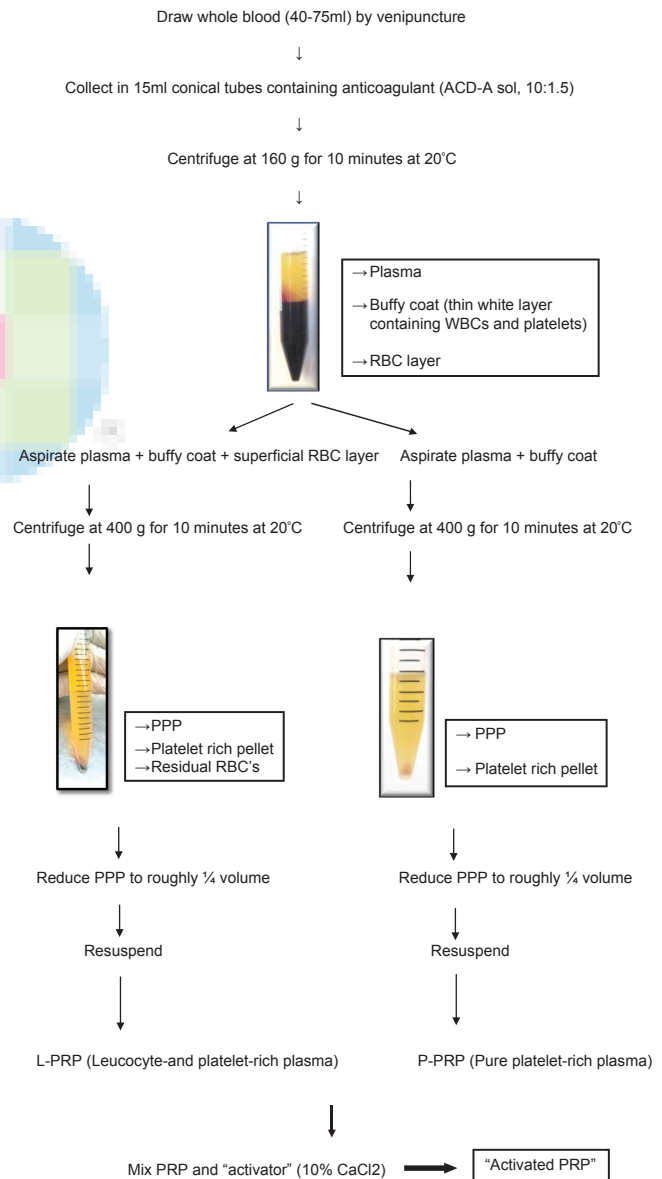
**Manual double spin method**

The American Association of Blood Banks technical manual,<sup>[7]</sup> states that “platelet-rich plasma is separated from whole blood by ‘light-spin’ centrifugation and subsequently the platelets are concentrated by ‘heavy-spin’ centrifugation with removal of the supernatant plasma.” The basic principle behind the PRP separation procedure is as follows.

The centrifugation process separates blood components owing to their different specific gravities, i.e., RBCs being the heaviest, followed by WBCs, whereas platelets are the lightest. The first centrifugation is slow to avoid spinning down platelets and to isolate plasma. Platelets are mostly concentrated right on top of the buffy coat layer. Subsequent centrifugation is faster, so that platelets are spun down and separate as a pellet at the bottom of the tube from platelet-poor plasma (PPP) above. The final platelet concentration depends on the volume reduction of PPP. Approximately 3/4 of the supernatant is discarded and the platelet-rich pellet is resuspended in remaining amount of plasma. The resulting

suspension is used as PRP. Calcium chloride (CaCl<sub>2</sub>) or thrombin can be used as an “activator” to trigger coagulation and hence degranulation of GFs to yield “activated PRP”. The procedure has been illustrated in a simplified flowchart in Figure 1.

The platelet yield depends mainly on conditional parameters like size and shape of the container used, rate and time of spin and anticoagulant used. There has been a gross lack of comparative studies to standardize the PRP procedural parameters. However, in our institution, we have adopted the centrifugation parameters used by Gonshor *et al*,<sup>[8]</sup> (as also mentioned in Figure 1) to obtain a desired platelet



**Table 1: Contents of PRP: Growth factors and their actions<sup>[4]</sup>**

PDGF- $\alpha\alpha$ , $\alpha\beta$ , $\beta\beta$	Chemotactic for fibroblasts and macrophages Mitogenic for fibroblasts, smooth muscle cells and endothelial cells
TGF $\alpha$ - $\beta$ 1, $\beta$ 2	Mediates angiogenesis Chemotactic for fibroblasts, keratinocytes and macrophages Mitogenic for fibroblasts and smooth muscle cells Inhibits endothelial cells, keratinocytes and lymphocytes Regulates matrix proteins, including collagen, proteoglycans, fibronectin and matrix-degrading proteins
VEGF $\dagger$	Chemotactic and mitogenic for endothelial cells Mediates angiogenesis
EGF $\ddagger$	Mediates angiogenesis Mitogenic for fibroblasts, endothelial cells and keratinocytes
HGF $\S$	Mediates regeneration
FGF $\parallel$	Mediates tissue organization and regeneration
FGF-9	Aids generation of new follicles

<sup>\*</sup>TGF: Transforming growth factor, <sup>†</sup>VEGF: Vascular endothelial growth factor, <sup>‡</sup>EGF: Epidermal growth factor, <sup>§</sup>HGF: Hepatocyte growth factor, <sup>||</sup>FGF: Fibroblast growth factor

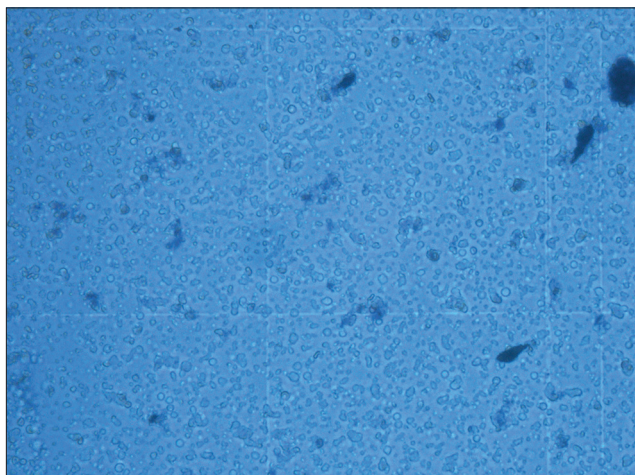
**Figure 1: Flowchart illustrating preparation of “activated PRP”**

concentration of four to seven times that of whole blood. The viability of the platelets is assured by carrying out the process in a refrigerated centrifuge at 20°C. Trypan blue staining can confirm the viable state of the platelet concentrate obtained by the above method, as shown in Figure 2.

The double spin method is preferred over the earlier prevalent single spin method,<sup>[9]</sup> as the therapeutic concentration of platelets was not achieved by the latter.<sup>[1]</sup> The active secretion of prepackaged GFs begins within 10 minutes of clot initiation and 95% of the secretion is completed within 1 hour.<sup>[10]</sup> Hence, PRP must be used on the treated site within 10 minutes of activation. The concentrated platelets remain viable for up to 8 hours and sterile if placed on a sterile surgical table.<sup>[6]</sup>

#### Automated devices

Numerous commercial devices of varying standards are now available for the preparation of PRP, but their application has been confusing because each technique leads to a different product with potentially dissimilar biology and unknown relative efficacy. In the section below, various devices and kits have been classified according to the product formed. Although time saving, these adapted kits can be quite expensive as compared to the manual process. Also, commercial interests tend to obscure the true clinical benefits of various platelet concentrates. Easy reproducibility of the product is also not consistent with the devices/kits. However, a prudent clinician needs to ensure the viability, concentration and activation of platelets obtained by the device used. Various devices have been approved by US Food and Drug Association (FDA)



**Figure 2: Smear showing concentrated viable platelets that do not take up the stain (Trypan blue, x20)**

e.g., Smart PRP<sup>®</sup> (Harvest Technologies Inc, Plymouth, MA), PCCS<sup>®</sup> (3i Implant Innovations Inc, West Palm Beach, FL), BioMet GPSII<sup>®</sup> etc.

#### “ALL PRP’S ARE NOT THE SAME”: CLASSIFICATION OF PLATELET CONCENTRATES

The development of a wide range of preparation protocols, devices and centrifuges for varying indications have led to a number of different platelet concentrates, unfortunately all under the same name as PRP. Ehrenfest *et al.*,<sup>[11]</sup> have proposed a classification of platelet concentrates into four categories depending upon their leucocyte and fibrin content as follows.

##### P-PRP (Pure platelet-rich plasma)

The P-PRP concentrate consists of an undetermined fraction of buffy coat, containing a large number of platelets, but most leucocytes are not collected. After the first slow spin centrifugation, only the superficial buffy coat layer is pipetted out and prepared for next centrifugation, as shown in Figure 1. E.g., Anitua's Plasma rich in growth factors (PRGF).

##### L-PRP (Leucocyte- and platelet-rich plasma)

L-PRP consists of most of the platelets, along with leucocytes and some residual RBCs, suspended in fibrin-rich plasma. It differs from P-PRP only on the means of buffy coat layer collection in which PPP along with the entire buffy coat layer and superficial 1-2 mm layer of RBCs are pipetted out [Figure 1]. E.g., Plateltex (Bratislava, Slovakia) and RegenACR<sup>®</sup> kit (Regen Laboratory, Mollens, Switzerland). These protocols employ gelifying agents or a separator gel within the centrifugation kit to enhance the complete collection of the buffy coat layer. Automated systems for L-PRP are PCCS and SmartPRP.

The manual PRP preparation process (as described above) is not clearly defined, it might randomly lead to P-PRP or L-PRP.

##### P-PRF (Pure platelet-rich fibrin)

The term PRF is used synonymously with platelet-rich fibrin matrix (PRFM). When P-PRP is mixed with activator and allowed to incubate for some time, a stable PRFM clot can be collected which has useful applications as described below. Very low amounts of leucocytes are collected owing to a specific separator gel used in the device. E.g., Fibrinet PRFM kit (Cascade Medical, NJ, USA).

### L-PRF (Leucocyte- and platelet-rich fibrin)

Here, blood is collected without any anticoagulant and immediately centrifuged. A natural coagulation process then occurs and three layers are formed: the RBC base layer, acellular plasma top layer and L-PRF clot in the middle, which harvests platelet and leucocyte growth factors into the fibrin matrix. There is no biochemical modification of the blood, i.e. no anticoagulants, thrombin or CaCl<sub>2</sub> are required. When pressed between two gauzes, the PRF clot becomes a strong membrane which also has potential applications. E.g., Choukroun's PRF.

### Concentration of PRP

The mean blood platelet level is 200,000 ± 75,000/μL. Although the PRP platelet count has not been optimized, a platelet concentration of more than 1 million/μL (approximately four to seven times the mean levels) is generally regarded as the therapeutically effective concentration of PRP.<sup>[1,12,13]</sup> Further, a bell-shaped response curve indicating a dose dependant nature has been shown to be associated with PRP.<sup>[14]</sup> Giusti *et al.*,<sup>[15]</sup> demonstrated that lower or higher concentrations than 1.5 million platelets/μL, seemed to inhibit the angiogenic potential in human endothelial cells. *In vitro* studies on dermal papilla cells have also supported PRP at concentrations of five to ten times the mean levels.<sup>[12]</sup> All the FDA-cleared PRP separator devices have been shown to achieve this therapeutic concentration of PRP.

## DERMATOLOGICAL INDICATIONS

Data analysed from peer-reviewed journals demonstrates a wide range of dermatological indications ranging from hair restoration to acne scarring as enumerated in Table 2.

### Androgenetic alopecia (AGA)

AGA is associated with a significant amount of psychosocial distress both in men and women. Much research has been done to expand the available therapeutic armamentarium. Hair transplantation has proven to be a boon for patients consenting for surgical procedures. Minoxidil and finasteride have an established efficacy in AGA, also as an adjuvant to hair transplantation. The angiogenic role of PRP has recently caught the attention of dermatologists and plastic surgeons, to explore its usefulness as a hair growth modality.

### Mechanism of action of PRP in AGA

Activated PRP stimulates proliferation and differentiation of stem cells in the hair follicle bulge area via multiple molecular mechanisms,<sup>[12]</sup> as mentioned in Table 3.

### Procedure

A proper informed consent, aseptic conditions and local anesthesia are important pre-requisites for the procedure. Patient must be free of anti-platelet drugs like aspirin or other non-steroidal anti-inflammatory drugs, for at least two weeks prior to the procedure. It has been used in a number of ways, based on personal preferences, both as an independent therapeutic modality or as an adjunct to hair transplantation to increase the survival of implanted grafts.

Various modes of PRP therapy for AGA are as follows:

1. Inter-follicular injection of PRP at the amount of 0.05-0.1 ml/cm<sup>2</sup>, in a retrograde fashion from deep to superficial, at every centimetre, throughout the treated site.
2. PRP mesotherapy: Scalp is punctured with microneedle roller of 1-mm fine needles followed by interfollicular injections of PRP (or by using mesogun) over the treated area and later, PRP is also sprayed on top of the scalp and left on overnight. It is usually done in 3 monthly sessions.
3. PRP can be used as an adjunct to hair transplantation:

**Table 2: Indications of PRP in dermatology**

Androgenetic alopecia <sup>[12,16-23]</sup>
Alopecia areata <sup>[20,24]</sup>
Skin rejuvenation <sup>[25-31]</sup>
Acne scars and contour defects <sup>[32-36]</sup>
Wound ulcers, Connective tissue disease associated ulcers <sup>[37-40]</sup>
Striae distensae <sup>[41,42]</sup>
Lipodermatosclerosis <sup>[43]</sup>
Lichen sclerosus <sup>[44]</sup>

**Table 3: Mechanism of action of PRP in AGA<sup>[12]</sup>**

Upregulation of transcriptional activity of β-catenin→Differentiation of stem cells into hair follicle cells
Increased bcl-2 levels→Anti-apoptotic→Prolongs survival of dermal papilla cells
Activation of Akt and ERK signalling pathways→Prolongs survival of dermal papilla cells
Expression of FGF-7 in dermal papilla cells→Prolongs anagen phase of hair cycle
Increased VEGF and PDGF→Proangiogenic→Increases peri-follicular vascular plexus

**Table 4: Evidence for the use of PRP in AGA**

Authors	Study design	Sample size	Level of evidence*	PRP preparation and conc.	Follow up	Results
Uebel <i>et al.</i> , <sup>[16]</sup> 2006	Open label right-left study comparing yield from follicular grafts imbibed in PRP vs saline, before implantation in FUT	n=20 (males)	II (a)	Manual double spin, Platelet conc. 4-6x†	7 m	Significant increase (3-52%) in yield of follicular units
Rinaldi <i>et al.</i> , <sup>[17]</sup> 2011	Double blind randomised trial to study effect of follicular grafts stored in PRP and <i>in vitro</i> evaluation of PRP vs Ringer's solution for storing transplanted grafts	n=100 (50 males, 50 females)	II (a)	Not mentioned	18 m	Significant effect (both <i>in vitro</i> and <i>in vivo</i> ) of PRP in preventing dermal papilla apoptosis, prolonging anagen phase and eventually stimulating hair re-growth in AGA without side effects
Li <i>et al.</i> , <sup>[12]</sup> 2012	<i>In vitro</i> study to illustrate molecular mechanisms of effect of PRP on hair growth and <i>in vivo</i> RCT with injections of PRP on mice	n=6 [2:PRP, 2:PBS† (control), 2:FBS‡ (positive control)]	I	Manual double spin, conc. 8.8x	3 weeks	Diffuse darkening of dorsal skin was observed after PRP injected once every 3 days for 2 weeks. At 3 weeks, near complete hair regrowth was observed.
Kang <i>et al.</i> , <sup>[18]</sup> 2011	Prospective open label controlled study comparing effect of interfollicular injections of CD34+ cell containing PRP vs placental extract (control)	n=26 (13 treated, 13 controls)	II (a)	Automated PRP device (SmartPReP) Conc. 5.9x	6 m	PRP showed significantly better improvement in hair thickness (P=0.027) and two-point score (P=0.023) than placental extract, but not in hair count (P>0.05)
Greco <i>et al.</i> , <sup>[20]</sup> 2009	Open label placebo controlled study to assess PRP mesotherapy in AGA	n=10, (5 treated, 5 controls)	II (a)	Not mentioned	8 m	9.7% increase in hair shaft diameter at 4 months and 6.1% at 8 months
Lopez <i>et al.</i> , <sup>[21]</sup> 2013	Open-label controlled study to assess effect of PRP mesotherapy in AGA	n=62 (31 treated, 31 controls)	III	Not mentioned in poster abstract	12 m	Significant (P=0.048) increase in hair density and borderline (P=0.053) increase in hair number
Park <i>et al.</i> , <sup>[22]</sup> 2012	Split scalp comparison of PRP injections vs saline in an AGA patient	n=1	III	PRP kit (Proslys; TOZAI Holdings, Inc., Seoul, Korea) Conc. Not documented	6 m	Significant increase in growth rate and hair density observed, but no change in hair thickness.
Takikawa <i>et al.</i> , <sup>[23]</sup> 2012	Prospective placebo controlled split-scalp study evaluating D/P as a new carrier in PRP for hair growth	n=26, [13: PRP and D/P vs saline, 13: PRP vs saline]	II (a)	Manual double spin method Conc. 6x	12 weeks	PRP and dalteparim/ protamine (D/P) provided additional increase in hair cross-section than PRP alone, although both facilitated hair growth than control side

\*Source: Department of Public Health Sciences King's College London, †PBS: Phosphate-buffered saline, ‡FBS: Fetal bovine serum

- The follicular grafts are dipped into PRP for about 15 minutes, before implantation so as to increase their survival rate after implantation.
- PRP is injected into the recipient area of scalp prior to or just after implantation of grafts.
- PRP is injected at and around the donor strip excision line, in follicular unit transplantation (FUT), to minimize bleeding, stimulate wound healing and reduce scarring.

**Evidence to support its use**

There is presently limited published data for this most widely used application of PRP in dermatology as summarized in Table 4. Most of the studies are open label with low to intermediate quality of evidence. In 2006, Uebel *et al.*,<sup>[16]</sup> were among the first to use PRP along with hair transplantation. They demonstrated an increase in the follicular density (range = 3-52%) after 7 months of FUT, by keeping follicular grafts in PRP for 15 minutes before implantation, with saline as the control. The increased survival of 2.4 follicular units per cm<sup>2</sup> implanted on the experimental side,

can be extrapolated as 240 units (or 480 follicles, assuming two follicles per unit) over a bald area of 100cm<sup>2</sup> (10 × 10 cm). This methodology can be advantageous especially in those patients with very thin and sparse hair in the donor area, so as to ensure the highest survival yield in implanted grafts. However, this trial was non-blinded and evaluation was done by manual counting of hair grafts (digital imaging was done in only 1 patient).

PRP as an incubation medium in FUT was also analyzed in a recent double-blind randomized controlled trial (RCT) on 100 AGA patients.<sup>[17]</sup> The investigators found reduction in diffuse hair loss and stimulated hair growth, without any untoward effects for a follow-up period of 18 months. *In vitro* evaluation also revealed that PRP could prevent dermal papilla apoptosis and prolong anagen phase of hair cycle.

The molecular pathways involved in the mitogenic effects of PRP have been well illustrated by Li *et al.*,<sup>[12]</sup> as mentioned in Table 3. In support to their *in vitro* data, authors demonstrated significant hair regrowth in treated mice, which further paved the way for its clinical application.

Kang *et al.*,<sup>[18]</sup> suggested that the CD34+ hematopoietic stem cells mobilized in peripheral blood and further concentrated in PRP prepared using Smart PRP<sup>®</sup>, could have synergistic effects on PRP-induced angiogenesis in patients with pattern hair loss. Their hypothesis was based on the previous evidence of angiogenic role of autologous CD34+ hematopoietic stem cells in ischemic conditions.<sup>[19]</sup>

PRP used as mesotherapy in AGA patients has also shown promising results. Open label studies by Greco *et al.*<sup>[20]</sup> and Lopez *et al.*,<sup>[21]</sup> observed a significant increase in hair diameter and hair density respectively, with this minimally invasive technique. An isolated report suggests the role of PRP therapy in patients intolerant to available medical therapies.<sup>[22]</sup>

### Modification of PRP

The ever increasing literature has also seen modifications of PRP to increase its therapeutic results. Takikawa *et al.*,<sup>[23]</sup> investigated a low-molecular weight heparin, as a carrier for PRP. Dalteparin/protamine (DP), in water soluble microparticles, acts as a biomaterial to adsorb, stabilize and gradually release the GFs in PRP, as almost all of them are known to be heparin

binding. Results showed that DP in PRP could further improve the hair thickness as compared to PRP alone without any side effects, although effect of DP alone was not assessed as control.

In view of the overall limited level of evidence of available literature, better designed, larger and long term trials are awaited. The question still remains, whether the clinical benefit achieved by PRP either as monotherapy or as an adjunct to surgical procedures, is worth the added resources and processing. Also, head to head comparative studies need to be performed between PRP and already established medical adjuvants. In view of relapse of pattern hair loss seen with early discontinuance of medical therapies, whether PRP can prove to be of any advantage is still a concern.

### Other alopecias: Alopecia areata, telogen effluvium

There is a clear paucity of published data in support of this application in alopecia areata and telogen effluvium. Greco *et al.*,<sup>[20]</sup> tried it in a single patient of alopecia areata as mesotherapy, with good subjective results at 10-months follow-up. Recently a randomized double blind, placebo and active controlled, half-head study evaluated PRP in 45 patients of alopecia areata. Monthly regimen for three sessions resulted in significant increase in hair regrowth and decrease in hair dystrophy and burning/itching sensation at 1-year follow-up, when compared with intralesional triamcinolone acetate or placebo.<sup>[24]</sup>

However, patients with alopecia areata and telogen effluvium, usually tend to have spontaneous remissions and respond well to commonly used medications, so it is difficult to attribute the regrowth of hair to PRP.

### Skin rejuvenation

Afresh PRP has been an emerging area of interest in aesthetic medicine. PRP has been reported to augment dermal elasticity by stimulating the removal of photodamaged extracellular matrix (ECM) components and inducing the synthesis of new collagen by dermal

**Table 5: Mechanism of action of PRP in skin rejuvenation**

Increased proliferation of human dermal fibroblasts
Increased expression of MMP*-1 and MMP-3→removal of photodamaged ECM
Increased production of procollagen type I peptide and expression of collagen type I, alpha-I→Synthesis of new collagen <sup>[25]</sup>
Increases expression of G1 cell cycle regulators→accelerates wound healing <sup>[26]</sup>

\*MMP: Matrix metalloproteinase

fibroblasts via various molecular mechanisms,<sup>[25,26]</sup> illustrated in Table 5.

### Procedure

Various methods have been tested for clinical use of PRP in skin rejuvenation, but a clearly defined method is unavailable.

1. Topical application under occlusion
2. Direct intradermal injections
3. As an adjuvant to lasers or microneedling. It is usually done once in every 4-6 months for 1 year and then yearly as maintenance therapy.<sup>[27]</sup>

### Evidence to support its use

Monthly intradermal injections of PRP in 3 sessions have shown satisfactory results in face and neck rejuvenation and scar attenuation.<sup>[28]</sup> Shin *et al.*,<sup>[29]</sup> showed that a combination of fractional non-ablative (erbium glass) laser therapy with topical application of PRP, resulted in objective improvement in skin elasticity, a lower erythema index and an increase in collagen density as well. Histological examination showed an increase in length of dermoepidermal junction, amount of collagen and fibroblasts in the treated skin.

PRP in combination with fractional ablative lasers (carbon dioxide) for deep wrinkles and severe photodamaged skin, has also been shown to reduce commonly encountered, transient adverse effects and decrease the downtime.<sup>[30]</sup> In a split face blinded trial, PRP injections given monthly for 3 months, have shown good results for infraorbital rejuvenation as well, without any obvious side effects.<sup>[31]</sup>

As varied number of products are available nowadays for skin rejuvenation like mesotherapy solutions, adipose derived stem cells etc., whether PRP can be used in combination with them to boost the aesthetic results, needs further clinical trials. Also, comparative studies are lacking to contrast PRP with other treatments like topical cosmeceutical preparations of growth factors, to be used after fractional laser resurfacing.

### Scars and contour defects

PRP has become a promising modality among soft tissue augmentation techniques. PRFM has been used as a filler to correct deep nasolabial folds without any adverse effects.<sup>[32]</sup> As an adjuvant, it has been studied with autologous fat transfer procedures. An *in vitro* pilot study, revealed that fat grafts when mixed with

PRP resulted in greater vascularity, fewer cysts and vacuoles, less fibrosis and overall improved survival and quality of fat grafts as compared to saline.<sup>[33]</sup> This novel regimen was found to maintain fat graft survival in a patient with facial contour defect for upto 2 years.<sup>[34]</sup> Data suggests that fat grafts can be admixed with PRP in treating traumatic scars, and further can be followed by fractional laser resurfacing to give best results.<sup>[35]</sup> PRP injections in combination with fractional carbon dioxide resurfacing have shown good results in acne scar resurfacing also, apart from skin rejuvenation.<sup>[36]</sup>

### Acute and chronic ulcers

The success of recombinant PDGF- $\beta\beta$  (becaplermin) gel in the treatment of diabetic neuropathic and other chronic wound ulcers,<sup>[37]</sup> has been translated into the potential use of PRP in the same. It can either be used as topical spray or as perilesional injections. PRFM, a viscous fibrin meshwork rich in GFs, has shown promising results when applied topically to the non-healing ulcers, to augment re-epithelialization.

Kim *et al.*,<sup>[38]</sup> treated 16 patients affected by various acute and chronic ulcers including stasis ulcers, diabetic ulcers, livedoid vasculitis, claw foot and traumatic ulcers with PRP. Topical application of PRP significantly accelerated the re-epithelialisation process, shown to be through the upregulation of cell cycle regulatory proteins like cyclin A and CDK4. Even dermatomyositis associated elbow ulcers have been successfully treated with PRP.<sup>[39]</sup>

However, in view of a small number of randomized controlled trials, most of which being either at high or unclear risk of bias, a recent review concluded that there is no current evidence to recommend the role of PRP for treating chronic wounds.<sup>[40]</sup>

### Striae distensae

The wound healing properties of PRP has also been applied in treating striae distensae Kim *et al.*,<sup>[41]</sup> treated 19 patients of striae, by employing an intradermal radiofrequency (RF) device, capable of delivering higher energy fluencies directly to the dermis, along with injecting PRP as a filler through its needle electrode. The thermal energy generated by bipolar RF, denatures the elastic fibres and collagen bundles and PRP stimulates wound healing, thereby providing synergistic benefits and good results. Transepidermal delivery of PRP using ultrasound has also been combined with fractional RF for treating

striae with post inflammatory pigmentation as the only reported side effect.<sup>[42]</sup>

### Lipodermatosclerosis

In an isolated case report, refractory lipodermatosclerosis was treated with intralesional subcutaneous injections of PRP in five sessions (fortnightly) that led to complete re-epithelialization of venous ulcer and marked improvement in hyperpigmentation and induration at the treated site.<sup>[43]</sup>

### Lichen sclerosis

Although the evidence is anecdotal, multilayer PRP injections used along with autologous fat transfer, deserves a special mention as a novel technique in the management of lichen sclerosis of vulva.<sup>[44]</sup>

### SAFETY OF PRP

True PRP is definitely autologous. Homologous platelets such as lyophilised donor platelets have no place in this field as they are antigenic by virtue of the abundance of cell membranes.<sup>[6]</sup>

The mitogenic effects of PRP are only limited to augmentation of the normal healing process and is theoretically not mutagenic, as the GFs released do not enter the cell or its nucleus, but only bind to the membrane receptors and induce signal transduction mechanisms.<sup>[45]</sup>

Being an autologous preparation, PRP is devoid of any serious adverse effects, apart from local injection site reactions like pain or secondary infection, which can be avoided with proper precautions. PRP has no issues regarding transmission of infections such as hepatitis-B, C or HIV. However, safety concerns with bovine thrombin have been raised about the potential transmission of Cruetzfeld-Jacob disease (mad-cow disease). These have been refuted by some stating that the prion vector has been found only in the neural tissues of cattle, whereas thrombin is solely isolated from the blood and is also further processed by heating.<sup>[6]</sup> Furthermore, reports of post-operative bleeding due to bovine thrombin-induced factor-V deficiency,<sup>[46]</sup> have made it an unpopular choice. On the other hand, use of  $\text{CaCl}_2$  as an activator, automatically eliminates the above risks. Newer alternatives like human recombinant thrombin, thrombin receptor agonist peptide (TRAP),<sup>[47]</sup> autologous thrombin (prepared simultaneously with some of the available kits) or type-I collagen<sup>[48]</sup> have been explored.

### FUTURE TRENDS

The next generation of autologous PRP is the addition of ECM and independent studies conclude that GF-ECM complexes may well be the most effective method to stimulate cell proliferation as well as tissue healing or regeneration. This GF-ECM complex has demonstrated a synergistic effect in both human and equine wounds and has future scope in hair research techniques.<sup>[49]</sup>

The role of PRP in addressing infection concerns in healing injuries is being widely investigated and holds promise, as reports of antibacterial nature of PRP are pouring in the literature.<sup>[50]</sup> Its bacteriostatic properties have been attributed to the antimicrobial proteins secreted by the platelets. The inclusion of leucocytes in PRP as in L-PRP with a potential benefit to combat infection and regulate immune function, is a matter of present debate.<sup>[11,50]</sup> Also, leucocytes produce large amounts of additional angiogenic factor VEGF, which is of crucial importance to the GF cocktail.<sup>[51]</sup> More studies are awaited to apply this novel concept to clinical practice.

### CONCLUSIONS

The potential role of PRP in dermatology and aesthetic medicine is an exciting frontier that may eventually lead to superior therapies in the near future, however according to the evidence based medicine, the level of evidence from the available published data is low. There are no double blind, randomized, placebo controlled trials conducted on a large sample size to constitute a good quality of evidence. Hence, a healthy amount of caution should be exercised by the treating physician in its preparation and use during procedures. Further research is awaited to unfold its long term efficacy and safety.

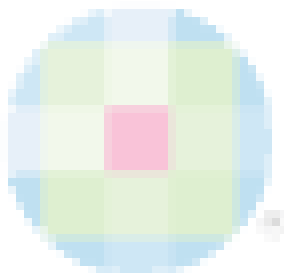
### REFERENCES

1. Marx RE, Garg AK. Dental and Craniofacial Applications of Platelet-Rich Plasma. Chicago: Quintessence Publishing; 2005.
2. Bhanot S, Alex JC. Current applications of platelet gels in facial plastic surgery. *Facial Plast Surg* 2002;18:27-33.
3. Takakura N, Yoshida H, Kunisada T, Nishikawa S, Nishikawa SI. Involvement of platelet-derived growth factor receptor-alpha in hair canal formation. *J Invest Dermatol* 1996;107:770-7.
4. Steed DL. The role of growth factors in wound healing. *Surg Clin North Am* 1997;77:575-86.
5. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: Growth factor enhancement for bone grafts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;85:638-46.
6. Marx RE. Platelet-rich plasma: Evidence to support its use.



- J Oral Maxillofac Surg 2004;62:489-96.
7. American Association of Blood Banks technical manual committee. Method 6.11: Preparation of platelets from whole blood. In: Vengelen-Tyler V, editor. AABB Technical Manual, 13<sup>th</sup> ed. Bethesda (MD): American Association of Blood Banks; 1999. p. 725.
  8. Gonshor A. Technique for producing platelet-rich plasma and platelet concentrate: Background and process. *Int J Periodontics Restorative Dent* 2002;22:547-57.
  9. Kurita M, Aiba-Kojima E, Shigeura T, Matsumoto D, Suga H, Inoue K, *et al.* Differential effects of three preparations of human serum on expansion of various types of human cells. *Plast Reconstr Surg* 2008;122:438-48.
  10. Kevy S, Jacobson M. Preparation of growth factors enriched autologous platelet gel. Proceedings of the 27<sup>th</sup> Annual Meeting of Service Biomaterials, April 2001. [Abstract]
  11. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol* 2009;27:158-67.
  12. Li ZJ, Choi HI, Choi DK, Sohn KC, Im M, Seo YJ, *et al.* Autologous platelet-rich plasma: A potential therapeutic tool for promoting hair growth. *Dermatol Surg* 2012;38:1040-6.
  13. Weibrich G, Kleis WK, Hafner G. Growth factor levels in the platelet-rich plasma produced by 2 different methods: Curasan-type PRP kit versus PCCS PRP system. *Int J Oral Maxillofac Implants* 2002;17:184-90.
  14. Krasna M, Domanović D, Tomsic A, Svajger U, Jeras M. Platelet gel stimulates proliferation of human dermal fibroblasts *in vitro*. *Acta Dermatovenerol Alp Panon Adriat* 2007;16:105-10.
  15. Giusti I, Rughetti A, D'Ascenzo S, Millimaggi D, Pavan A, Dell'Orso L, *et al.* Identification of an optimal concentration of platelet gel for promoting angiogenesis in human endothelial cells. *Transfusion* 2009;49:771-8.
  16. Uebel CO, da Silva JB, Cantarelli D, Martins P. The role of platelet plasma growth factors in male pattern baldness surgery. *Plast Reconstr Surg* 2006;118:1458-66.
  17. Rinaldi F, Sorbellini E, Coscera T. The role of platelet rich plasma to control anagen phase: Evaluation *in vitro* and *in vivo* in hair transplant and hair treatment. *Int J Trichol* 2011;3:S14-5.
  18. Kang JS, Zheng Z, Choi MJ, Lee SH, Kim DY, Cho SB. The effect of CD34+ cell-containing autologous platelet-rich plasma injection on pattern hair loss: A preliminary study. *J Eur Acad Dermatol Venereol* 2012. [In press]
  19. Mackie AR, Klyachko E, Thorne T, Schultz KM, Millay M, Ito A, *et al.* Sonic hedgehog-modified human CD34+ cells preserve cardiac function after acute myocardial infarction. *Circ Res* 2012;111:312-21.
  20. Greco J, Brandt R. The effects of autologous platelet rich plasma and various growth factors on non-transplanted miniaturized hair. *Hair Transplant Forum Int* 2009;19:49-50.
  21. Lopez V, Vaya A, Bautista D, Ricart JM. Autologous platelet-rich plasma as a potential therapeutic tool in androgenetic alopecia. *J Am Acad Dermatol* 2013;68:SAB103.
  22. Park KY, Kim HK, Kim BJ, Kim MN. Platelet-rich plasma for treating male pattern baldness. *Dermatol Surg* 2012;38:2042-4.
  23. Takikawa M, Nakamura S, Nakamura S, Ishirara M, Kishimoto S, Sasaki K, *et al.* Enhanced effect of platelet-rich plasma containing a new carrier on hair growth. *Dermatol Surg* 2011;37:1721-9.
  24. Trink A, Sorbellini E, Bezzola P, Rodella L, Rezzani R, Ramot Y, *et al.* A randomized, double-blind, placebo and active-controlled, half-head study to evaluate the effects of platelet rich plasma on alopecia areata. *Br J Dermatol* 2013. [In press]
  25. Cho JW, Kim SA, Lee KS. Platelet-rich plasma induces increased expression of G1 cell cycle regulators, type I collagen, and matrix metalloproteinase-1 in human skin fibroblasts. *Int J Mol Med* 2012;29:32-6.
  26. Kim DH, Je YJ, Kim CD, Lee YH, Seo YJ, Lee JH, *et al.* Can platelet-rich plasma be used for skin rejuvenation? Evaluation of effects of platelet-rich plasma on human dermal fibroblast. *Ann Dermatol* 2011;23:424-31.
  27. Konda D, Thappa DM. Mesotherapy: What is new? *Indian J Dermatol Venereol Leprol* 2013;79:127-34.
  28. Redaelli A, Romano D, Marcianó A. Face and neck revitalization with platelet-rich plasma (PRP): Clinical outcome in a series of 23 consecutively treated patients. *J Drugs Dermatol* 2010;9:466-72.
  29. Shin MK, Lee JH, Lee SJ, Kim NI. Platelet-rich plasma combined with fractional laser therapy for skin rejuvenation. *Dermatol Surg* 2012;38:623-30.
  30. Na JI, Choi JW, Choi HR, Jeong JB, Park KC, Youn SW, *et al.* Rapid healing and reduced erythema after ablative fractional carbon dioxide laser resurfacing combined with the application of autologous platelet-rich plasma. *Dermatol Surg* 2011;37:463-8.
  31. Kang BK, Lee JH, Shin MK, Kim NI. Infraorbital rejuvenation using PRP (platelet-rich plasma): A prospective, randomized, split-face trial. *J Am Acad Dermatol* 2013;68:SAB24.
  32. Sclafani AP. Platelet-rich fibrin matrix for improvement of deep nasolabial folds. *J Cosmet Dermatol* 2010;9:66-71.
  33. Oh DS, Cheon YW, Jeon YR, Lew DH. Activated platelet-rich plasma improves fat graft survival in nude mice: A pilot study. *Dermatol Surg* 2011;37:619-25.
  34. Park KY, Kim IS, Kim BJ, Kim MN. Letter: Autologous fat grafting and platelet-rich plasma for treatment of facial contour defects. *Dermatol Surg* 2012;38:1572-4.
  35. Cervelli V, Nicoli F, Spallone D, Verardi S, Sorge R, Nicoli M, *et al.* Treatment of traumatic scars using fat grafts mixed with platelet-rich plasma, and resurfacing of skin with the 1540 nm nonablative laser. *Clin Exp Dermatol* 2012;37:55-61.
  36. Lee JW, Kim BJ, Kim MN, Mun SK. The efficacy of autologous platelet rich plasma combined with ablative carbon dioxide fractional resurfacing for acne scars: A simultaneous split-face trial. *Dermatol Surg* 2011;37:931-8.
  37. Smiell JM, Wieman TJ, Steed DL, Perry BH, Sampson AR, Schwab BH. Efficacy and safety of becaplermin (recombinant human platelet-derived growth factor-BB) in patients with nonhealing, lower extremity diabetic ulcers: A combined analysis of four randomized studies. *Wound Repair Regen* 1999;7:335-46.
  38. Kim SA, Ryu HW, Lee KS, Cho JW. Application of platelet-rich plasma accelerates the wound healing process in acute and chronic ulcers through rapid migration and upregulation of cyclin A and CDK4 in HaCaT cells. *Mol Med Rep* 2013;7:476-80.
  39. Ralliss E, Falidas E, Villias C. Amyopathic dermatomyositis-associated bilateral elbow ulcers successfully treated with autologous platelet-rich plasma. *Int J Dermatol* 2013. [In press]
  40. Martinez-Zapata MJ, Marti-Carvajal AJ, Solà I, Expósito JA, Bolívar I, Rodríguez L, *et al.* Autologous platelet-rich plasma for treating chronic wounds. *Cochrane Database Syst Rev Online* 2012;10:CD006899.
  41. Kim IS, Park KY, Kim BJ, Kim MN, Kim CW, Kim SE. Efficacy of intradermal radiofrequency combined with autologous platelet-rich plasma in striae distensae: A pilot study. *Int J Dermatol* 2012;51:1253-8.
  42. Suh DH, Lee SJ, Lee JH, Kim HJ, Shin MK, Song KY. Treatment of striae distensae combined enhanced penetration platelet-rich plasma and ultrasound after plasma fractional radiofrequency. *J Cosmet Laser Ther* 2012;14:272-6.
  43. Jeong KH, Shin MK, Kim NI. Refractory lipodermatosclerosis treated with intralesional platelet-rich plasma. *J Am Acad Dermatol* 2011;65:e157-8.
  44. Casabona F, Priano V, Vallerino V, Cogliandro A, Lavagnino G. New surgical approach to lichen sclerosis of the vulva: The role of adipose-derived mesenchymal cells and platelet-rich plasma in tissue regeneration. *Plast Reconstr Surg* 2010;126:e210-1.
  45. Schmitz JP, Hollinger JO. The biology of platelet-rich plasma. *J Oral Maxillofac Surg* 2001;59:1119-21.
  46. Cmolik BL, Spero JA, Magovern GJ, Clark RE. Redo cardiac surgery: late bleeding complications from topical thrombin-induced

- factor V deficiency. J Thorac Cardiovasc Surg 1993;105:222-7.
47. Landesberg R, Burke A, Pinsky D, Katz R, Vo J, Eisig SB, *et al*. Activation of platelet-rich plasma using thrombin receptor agonist peptide. J Oral Maxillofac Surg 2005;63:529-35.
  48. Fufa D, Shealy B, Jacobson M, Kevy S, Murray MM. Activation of platelet-rich plasma using soluble type I collagen. J Oral Maxillofac Surg 2008;66:684-90.
  49. Clark RA. Synergistic signaling from extracellular matrix-growth factor complexes. J Invest Dermatol 2008;128:1354-5.
  50. Anitua E, Alonso R, Girbau C, Aguirre JJ, Muruzabal F, Orive G. Antibacterial effect of plasma rich in growth factors (PRGF®-Endoret®) against *Staphylococcus aureus* and *Staphylococcus epidermidis* strains. Clin Exp Dermatol 2012;37:652-7.
  51. Werther K, Christensen IJ, Nielsen HJ. Determination of vascular endothelial growth factor (VEGF) in circulating blood: Significance of VEGF in various leucocytes and platelets. Scand J Clin Lab Invest 2002;62:343-50.



## Conference Notice

**“LEPCON 2014”, March 28-30, 2014.**

**29<sup>th</sup> Biennial Conference of Indian Association of Leprologists**

**Conference Venue: Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, India.**  
[pgimer.edu.in](http://pgimer.edu.in)

**The abstract submission deadline is January 30, 2014.**

**Submit your abstracts by E-mail at:**

**[lepcon2014@gmail.com](mailto:lepcon2014@gmail.com)**

**For more information: [www.lepcon2014.com](http://www.lepcon2014.com)**

Conference Highlights:

- CME theme – Sustaining Leprosy Elimination
- Workshop – Practical aspects of Leprosy
- Award paper session & Quiz for PG students
- CME credit hours
- Expert National & International Faculty
- Dermatologists role in emerging scenario
- Supporting Organizations: ICMR, DGHS, IAL, ILA, ILEP, WHO

**Contact address:** Dr. Sunil Dogra

Organizing Secretary – LEPCON 2014

Department of Dermatology, Venereology & Leprology

Room no 8, First Floor, D- Block, Faculty Offices, Nehru Hospital

Postgraduate Institute of Medical Education & Research

(PGIMER), Sector 12, Chandigarh, 160 012, India

Ph: 0172-2756552/2756559 (O). 9855005941 (M)

E mail: [lepcon2014@gmail.com](mailto:lepcon2014@gmail.com)

[www.lepcon2014.com](http://www.lepcon2014.com)

Copyright of Indian Journal of Dermatology, Venereology & Leprology is the property of Medknow Publications & Media Pvt. Ltd. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.