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Autologous Platelet Rich Plasma as a Treatment of Male Androgenetic Alopecia: Study of 14 Cases

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Abstract

In this study, we report 14 cases of androgenetic alopecia (AGA) in men treated by autologous platelet rich plasma (PRP). Each patient had several injections of non-activated PRP (PRPn) on the sclap. The quantitative assessment of hair density was performed by hair count with TrichoScan and the cosmetic assessment by Canfield stereotaxic system (Standardized photographs seen by 3 independent assessors). A slight improvement of hair density was observed in 11 cases while a cosmetic improvement on the vertex was noticed only in 2 cases according to 3 assessors.

Keywords: Platlet rich plasma; Male androgenetic alpoecia; Hair density

Introduction

Autologous PRP has been used since 2004 [1] in Orthopedics and since 2010 [2] in Rheumatology. In Dermatology, It has been used for the treatment of acne scars, wounds and ulcers [3,4] as well as in hair surgery [5]. Its use in the treatment of hair diseases is recent. Trink and al. first showed the possible interest of PRP in alopecia areata [6].

Studies made with PRP suggest the repairing and regenerative role of various growth factors released by platelet alpha granules after their activation. These growth factors, especially PDGF, TGFβ1, EGF, FGF and IFG1 stimulate cell proliferation and cell differentiation, chemotactism and angiogenesis [7,8].

VEGF activates angiogenesis and hair growth and increases the hair follicle size. In mice, the increase of perifollicular vessels during anagen phase is associated with the increase of VEGF and the decrease of perifollicular vessels during catagen phase is associated with the decrease of VEGF [9]. FGF2, TGFβ and PDGF induce cell proliferation in cartilage and bone [10,11].

Some studies showed the role of growth factors released by platelet alpha granules as a PDGF, TGF, VEGF and IGF in the stimulation of human dermal fibroblasts and their possible role in skin rejuvenation [12-14].

A more recent study highlights the increase of β Catenine and FGF activities in dermal papilla due to stimulation by PRP. These two factors are two important stimuli in hair growth. PRP would accelerate the transition from telogen to anagen phase [15].

Based on these data on the PRP impact on dermal papilla and its potential effects on hair cycle, we decided to study its efficiency in the treatment of male androgenetic alopecia.

As in androgenic alopecia there is a progressive miniaturization of hair follicle and the anagen phase becomes shorter at each cycle and hair follicle size smaller, we wondered if the regenerative feature of PRP and its growth factors can reverse or delay the progress of disease in AGA.

Patients and Methods

Study: It was an open monocentric and prospective study on 14 men aged from 18 to 60 years old with AGA. All patients provided written consent before participating in the study, which was performed according to the Declaration of Helsinki.

Patients: 17 male patients (age range: 18-60) with AGA were treated (IIv to VI Norwood-Hamilton classification) [16]. 12 patients had never had any treatment in the past and 5 patients had been treated with Minoxidil (patients 8, 12, 15 and 17) or Finasteride (patients 2 and 12). These treatments were stopped 6 months before the study (Table 1).

5 patients were Non-European and 12 European. AGA began at the age of 17 in 3 patients, between 20-25 in 5 patients, between 28-32 in 4 patients and at the age of 40 in 2 patients. AGA progress was very long (13 to 20 years) in 4 patients, 6 years in one patient and 2 to 4 years in 7 others.

Treatment: Each patient received 4 series of injections (4 to 5 ml per session) of PRP non-activated (PRPn). Patients were treated at W0, W3, W6 and W12 (every 3 weeks for 3 first injections and 6 weeks for the last injection). The assessment was done at W16, 4 weeks after the last session.

Patients' blood samples were taken for the injections. To prepare PRPn, 8 ml of peripheral blood was obtained in each session (Regen Lab device) and centrifuged at 3400 rpm for 5 minutes. The platelet poor plasma (PPP) and PRP separated by gel, are extracted and mixed obtaining 4 to 5 ml PRPn which was injected regularly in superficial dermis over the vertex. Every injection consisted of 0.05 to 0.1 ml of PRPn using a 32G needle.

Assessment criteria: Quantitative: Hair density and hair count were assessed by TrichoScan in a fixed circular surface (0.65 cm^2) located by semi-permanent tattoos and pictures from video-microscopy provided comparison before and after the treatment (S0 and S16).

Cosmetic: The assessment was done comparing standardized digital photographs taken before and after the treatment (S0 and S16). These photographs were made by Canfield stereotaxic system [17]. One angle of incidence of the frontal anterior zone and the other, the vertex. Three assessors (2 independent) noted the qualitative change of hair using a scale of 7 scores.*

*Scale based on 7 scores (-3: highly decreased, -2: moderately decreased, -1: slightly decreased, 0: unchanged, 1: slightly increased, 2: moderately increased, 3: highly increased.)

Self-assessment: a self-assessment questionnaire based on 5 criteria was filled by each patient: change in hair texture (quality), change in volume, shedding decrease, pigmentation and grow back. Also another questionnaire regarding the quality of life (DLQI) before and after treatment (S0 and S16) was filled by patients.

Patient	Noorwid-Hamilton Classification scale	Age	Treatment prior to study	Platelets (peripheral blood)	Disease-onset (year-old)	Ethnic group
1	V	31	NO	200 G/l	17	European
3	IIv	20	NO	259 G/l	17	European
4	IIv	24	NO	233 G/l	20	European
5	Female pattern	23	NO	231 G/l	17	Asian
6	III Vertex	33	NO	210 G/l	28	European
7	VI	59	NO	190 G/l	40	European
8	IV	43	Minoxidil	223 G/l	30	European
9	Female pattern	28	NO	240 G/l	25	European
11	IV	58	NO	220 G/l	40	European
12	IV	25	Minoxidil +Finasteride	220 G/l	22	European
13	Female pattern	36	NO	169 G/l	32	Arabian
14	III	31	NO	253 G/l	28	Pakistani
15	III	36	Minoxidil	190 G/l	32	European
17	III	28	Minoxidil	211 G/l	23	European
2	III	25	Finasteride	250 G/l	22	European
10	III	24	NO	219 G/l	22	African
16	Female pattern	32	NO	311 G/l	29	Asian

Table 1: Patients' characteristics at baseline.

Results

2 of 17 patients included interrupted the study for personal reasons after 2 and 3 injections (travelling…). One patient was retreated from the follow-up after the treatment. Finally 14 patients enrolled into the study, completed the treatment and were assessed at W0 and W16.

Quantitative assessment

Mean hair density varies from 128.7 (at W0) to131.9 (at W16). The mean increase of density is 3.1/0.65 cm^2 or 2.9% (Table 2).

TrichoScan assessment showed an increase in hair density in 11 patients (+0.50% to +10%). Gain in hair number was more than 7% in 3 patients. We observed a decrease of hair density in 3 patients (-1.44 % to -1.72%). Globally the number of new hair follicles was 33 and the number of vellus hairs was 16 in our study.

Hair Count (W0; W16)*				
Patients	**Hair Gain**	**Hair density (W0)**	**Hair density (W16)**	**W0-W16**
1	**1.57**	190	193	3
3	**2.17**	138	141	3
4	**0.50**	198	199	1
5	**0.85**	117	118	1
6	**2.65**	151	155	4
7	**3.38**	59	61	2
8	**-1.44**	69	68	-1
9	**-1.72**	116	114	-2
11	**10**	80	88	8
12	**0.94**	212	214	2
13	**7.22**	83	89	6
14	**7.43**	121	130	9
15	**8.26.**	150	160	10
17	**-1.68**	119	117	-2
MEAN	**2.9**	**128.8**	**131.9**	**3.1**
Standard Deviation		**47.9**	**48**	**3.9**
2		154	Study interrupted	
10		119	Study interrupted	
16		114	Study interrupted	
*Surface of measured hair density: 0.65 cm^2				

Table 2: Hair density measured before and after treatment by TrichoScan™.

Cosmetic assessment

Vertex photographs showed a slight improvement in 2 cases according to 3 assessors and in one case according to only 1 assessor; a worsening was observed in 6 cases and 2 cases remained unchanged (Tables 3a) (Figures 1 and 2).

Frontal photographs showed a slight improvement in 2 cases according to 3 assessors and in 3 cases according to only 1 assessor; a worsening was observed in 2 cases and 7 cases remained unchanged.

Patients	Incidence	Comparison W0/W16			
		Assessor 1	Assessor 2	Assessor 3	Mean
1	Frontal	-1	-1	0	-0.7
	Vertex	0	0	0	0
3	Frontal	0	0	0	0
	Vertex	0	0	0	0
4	Frontal	1	1	1	1
	Vertex	0	-1	0	-0.3
5	Frontal	0	0	0	0
	Vertex	1	1	1	1
6	Frontal	0	0	0	0
	Vertex	-1	-1	0	-0.7
7	Frontal	0	0	0	0
	Vertex	1	1	1	1
8	Frontal	0	0	0	0
	Vertex	-2	-2	-1	-1.7
9	Frontal	0	0	0	0
	Vertex	0	-1	0	-0.3
11	Frontal	0	0	1	0.3
	Vertex	0	0	0	0
12	Frontal	0	0	0	0
	Vertex	0	-1	-1	-0.7
13	Frontal	0	0	1	0.3
	Vertex	0	0	0	0
14	Frontal	1	1	1	1
	Vertex	0	0	1	0.3
15	Frontal	0	0	1	0.3
	Vertex	-1	-1	-1	-1
17	Frontal	0	-1	0	-1
	Vertex	-1	-1	0	-0.7

Table 3a: Clinical assessment by 3 assessors.

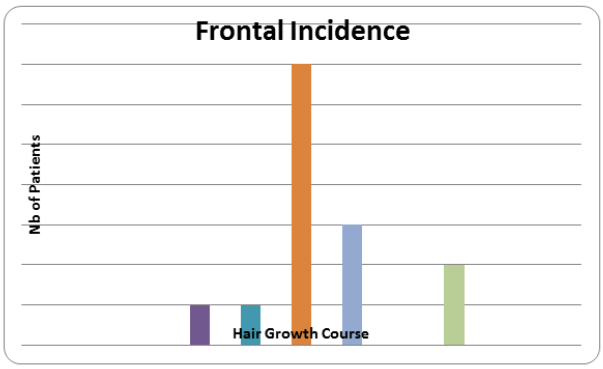

Figure 1: Chart: Frontal incidence (clinical assessment by 3 assessors).

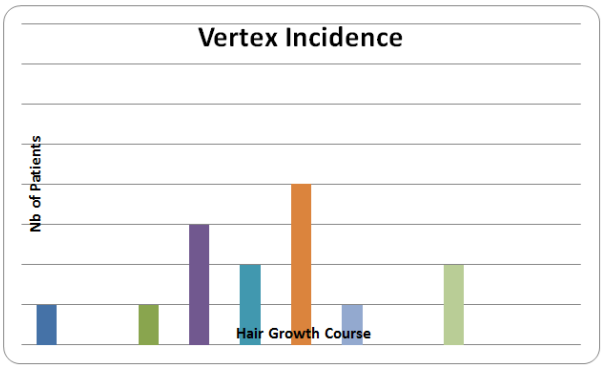

Figure 2: Chart: Vertex incidence (Clinical assessment by 3 assessors).

Self-assessment questionnaires showed

- An improvement of texture 14 times (100%)
- An improvement of volume 5 times (35.7%).
- A decrease of shedding 10 times (71.4%)
- A growth back 7 times (50%).

In 2 patients with blond hair, we observed a slight pigmentation in the treated zone (Table 4).

Patients	Better texture	Better volume	Shedding stop	Hair regrowth	Pigmentation
1	+		+	+	+
3	+ +	+ +		+ +	
4	+			+	+
5	+ + +	+	+	+ +	
6	+		+		
7	+ +			+	

8	+ +		+		
9	+				
11	+ + +	+	+ +	+	
12	+ + +	+	+		
13	+		+		
14	+ +		+ +		
15	+	+	+		
17	+		+	+	

+ : slight change
++ : moderate change
+++ : significant change

Table 4: Patients self-assessments.

Questionnaires of quality of life before and after treatment show a slight improvement of quality of life in 8 patients

Patients	1	3	4	5	6	7	8	9	11	12	13	14	15	17
Before treatment	0	0	0	0	0	0	0	4	0	1	5	0	0	0
After Treatment	1	0	0	2	0	0	2	6	1	5	10	2	0	2

Table 5: Dermatology life quality index before and after treatment (DLQI).

Discussion

Even though our study was conducted without a control group, it does not totally confirm the interest for the use of PRP in AGA already mentioned in two previous studies [18,19].

Our study showed an increase in hair density in 11 out of 14 patients who completed the treatment. This change is slight though (2.9%). In 3 cases of 14, it is higher than 7% and could be compared to results obtained by reference treatments of AGA like Minoxidil and Finasteride [20,21]. Topical Minoxidil 5% (foam) induced a mean increase of hair count of 13.4% in 16 weeks and Finasteride (oral) 1 mg/day induced a mean increase of hair density of 11% in 12 months [21].

In the specific conditions of this study our results are less positive than the ones of these two reference treatments of AGA. We observed that 3 of 4 best responders were 31 to 36 -year-old and the best response was seen in AGA stage III to IV. Among the best responders, 3 patients had a very recent history of AGA (less than 4 years).

The hair density measurement was done only in vertex in the same zone in each patient (equal distance between two ears). We did not measure the hair density in frontal area and we do not know if the PRP acts differently in this zone.

The cosmetic assessment results with global photographs are disappointing, and in this study the hair density did not allow to obtain cosmetically attractive results. Nevertheless, the clinical self-assessment of patients showed a better hair texture in all cases and a better growth back for half of them, as well as the interruption of shedding in more than half of patients.

In this study, we used a regular injection technique covering all the vertex and the frontal area(4 to 5ml of PRPn) in contrast with other studies where only a limited area was treated so that , in these studies the biologically active product in this limited zone is concentrated and probably increases the effectiveness of the treatment [22].

Cervelli and al. have treated a group of male patients with AGA and have obtained a mean gain of 27.7 hair/cm 2 or 19.41% [22]. Another recently published study used a large volume of peripheral blood (60ml) and obtained high platelet concentrations (6 or 7 fold more than peripheral blood) leading to better results [18]. This last study showed an improvement of hair volume in early AGA in men and women but the PRP was rich in leucocytes and the assessment was done through photographs without hair counting, hence it is subject to criticism [18].

The use of PRP and the assessment of its effects raise issues of definition and exact determination of its content. Regarding its nature, in this study we used non activated PRP (without adding Calcium Gluconate or Calcium Citrate) considering that the centrifugation, also intradermal injections (micro blood vessels injuries), and the contact with dermal fibroblasts would be sufficient to activate platelets and to release growth factors [12,14,23]. The activated PRP (PRPa) is obtained by adding Calcium Gluconate to PRPn which triggers the release of growth factors by platelet α-granules. Therefore PRPa could be associated with increased production of growth factors which in turn would show more efficacy.Two studies [6,22] using PRPa in two different indications had interesting results: Cervelli and al. using PRPa in AGA obtained almost.

19% of gain in mean hair density while Trink and al. using PRPa in alopecia areata noticed better results compared to patients treated with 2.5mg/ml of Triamcinolone acetonide (60% of complete remission compared to 27%). This suggests that PRPa could be more efficient than PRPn. Consequently it would be interesting to perform a study comparing these two types of PRP.

Regarding its content, it is essential to measure after centrifugation and before injection in each session, platelet concentration and ideally growth factors to assess both the quality and the quantity of what to inject. We know that there are a wide range of devices on the market (16 various systems without counting blood banks and private laboratories) and the heterogeneity of these systems leads to a large variability of platelet and growth factors concentrations, thus making any comparison impossible. A recent study compared this variability between 5 systems and the authors propose to use “platelet dose” as a terminology to standardize the technique and determine platelet concentration of PRP. In fact, the quantity of injected cells is the only parameter correlated to clinical efficacy as shown with bone marrow transplant in hematology [25]. They propose the following formulas:Injected platelet dose in PRP (X 10)=volume of PRP obtained (ml) × Platelet concentration in PRP (G/ml)/1000

Growth factor dose (pg)=volume of PRP obtained (ml) × Growth factors concentration in PRP (pg/ml)

We know there is a positive correlation between platelet dose and growth factor dose for all growth factors (VEGF, PDGF, EGF, TGFβ1) [24]. Another interesting notion is “platelet capture efficacy” that correlates obtained platelet concentration in the sample with platelet

concentration in peripheral blood. These notions allow to biologically characterize the obtained PRP.

Once PRP biologically characterized, we have to determine the optimal platelet concentration for each indication. The optimal concentration is different for each tissue. For example for Achilles tendinopathy or bone surgery (anterior cruciate ligament) the optimal concentration is 1 to 6 fold more than peripheral blood concentration [26,27]. In studies done in dermatology, the platelet concentration was 1.6 fold more than in peripheral blood. Once we have determined the optimal platelet dose, we can resolve the problem of volume to inject, because the volume depends on platelet dose contained in one ml of PRP.

Another aspect consists of taking into consideration the half-life of platelets (7 to 10 days) and to perform more frequent sessions to maintain long lasting stimulation by growth factors in dermis, especially when we use a small amount of PRPn.

Nevertheless, It is important to determine the frequency and the number of sessions not only based on half-life of platelets but also up to patient background. The role of age, AGA staging and probably correlation with androgenic activity may be considered. These factors could interfere with PRP efficiency. For example, in a young subject, the regenerative capacity is high but androgenic activity is equally high. These two factors can thwart variously and alter PRP efficacy. One the other hand AGA staging and disease progress are important. PRP seems to be less effective in late AGA and/or rapidly progressing AGA.

In this study we observed a few side effects such as erythema or headaches. Two patients with seborrheic dermatitis noticed an improvement with PRP (probably anti-inflammatory effect?) and we observed a darkening of treated hair in two patients with blond hair.

We did not realize biopsies as Cervelli and al. did. In their study, scalp biopsies showed the increase of hair follicle number and the increase of epidermis thickness confirming clinical data and dermoscopic measurements [22]. The angiogenic role of PRP in endothelial cells is known at high concentration (1500000 platele/µl) [28]. It would be interesting to realize further studies to measure molecular and cellular effect of PRP in scalp and skin.

Kang et al. obtained better results in AGA in male and female patients by adding bone marrow derived $CD34^+$ cells to activated PRP but this study does not permit to assess the efficiency of PRP solely. This technique deserves further studies [29].

Unlike the conventional treatments of AGA, our approach does not require long term therapy, potential side effects and/or high degree of compliance.

Patients' compliance is not always very high with Minoxidil, because of cosmetic effects and long term use. Also Finasteride has raised concerns for some patients regarding its sexual side effects (decreased libido, hypofertility). PRP as an autologous and non-chemical treatment is better accepted by patients who wish to avoid these disadvantages.

Consequently for non-responders to these therapies, PRP can be an alternative. Also as the mechanism of action of PRP is different from the two other treatments, we may have an additional positive effect by using PRP in responders to Minoxidil and Finasteride. In terms of costs, PRP may be more cost effective in long term than conventional therapies.

To summarize, despite the disappointing photographic results, our study seems to confirm the potential interest of the use of PRP in AGA as mentioned in previous studies [18,19,22] (Figures 3-5).

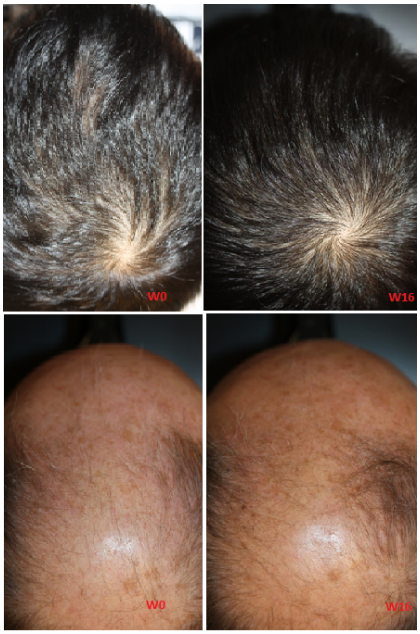

Figure 3: Clinical photographs (vertex).

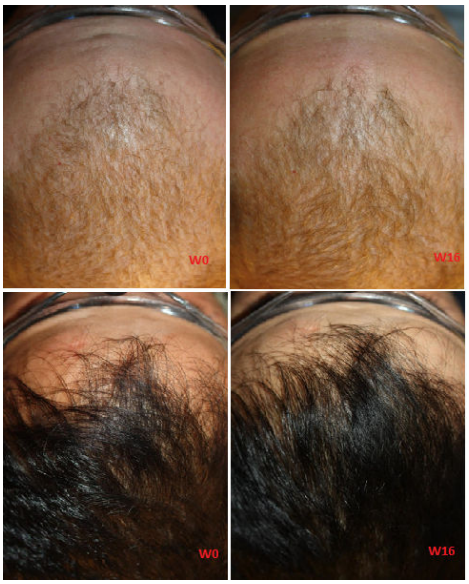

Figure 4: Clinical photographs (frontal).

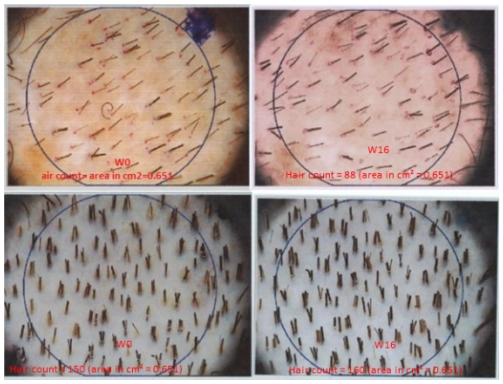

Figure 5: Hair count.

There is an objective improvement of hair density in the majority of patients, but this is not sufficient (in the conditions of our study) to induce a cosmetically visible improvement. The treatment seems to have a stabilizing effect. To optimize the hair growth it is necessary to:

- Realize complementary studies to better determine the injected platelet dose and the optimal platelet concentration and volume to inject.
- Shorten intervals between injection sessions.
- Realize a study comparing PRPa and PRPn.
- Select the following responders : young subjects (less than 40-year-old), early staging (stage III to V), recent AGA (less than 4 years of progress)

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