



**ORIGINAL ARTICLE**

## Follicular Unit Extraction with or without Platelet Rich Plasma in the Treatment of Androgenic Alopecia.

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**ABSTRACT**

**Background:** Hair transplant surgery using follicular unit extraction technique (FUE) is a common surgical procedure for the treatment of prominent hair loss. This study aimed to determine the role of Platelet Rich Plasma (PRP) in the procedure of Follicular Unit Extraction (FUE).

**Patients and methods:** A prospective comparative study was carried out in Plastic & Reconstructive Surgery Department of Zagazig University Hospitals during the period from January 2019 to January 2020. It included 16 patients with androgenic alopecia, patients included in the study was divided into two groups according to receiving RPR or not, Group (1); eight Patients treated with FUE with PRP. Group (2); eight Patients treated with FUE without PRP. The median age and degree of medical comorbidities were comparable in the two groups. Hair density indices were compared using Trichoscope.

**Results:** All eight patients treated with PRP showed a good hair regrowth, with prefect outcome. Of the eight patients treated without PRP, five showed a good hair regrowth, with good outcome.

**Conclusion:** This study demonstrated that PRP treatment during the hair transplant plays a significant role in hair re-growth, and it remarkably improves density and quality of hair growth.

**Key words:** Follicular Unit Extraction; Platelet Rich Plasma; Androgenetic Alopecia.



**INTRODUCTION**

Hair loss, alopecia or baldness refers to loss of scalp hair of varying severity, age of onset and pattern. There are different subtypes of hair loss-related disorders including androgenetic alopecia (AGA), alopecia areata (AA), telogen effluvium or scarring alopecia that differ in their pathophysiological and etiological characterization as well as in their genetic pattern and biomolecular mechanisms[1].

Alopecia is more prevalent in men than in women (70% and 40%, respectively), but psychological disturbance has been reported in both genders including psychiatric symptoms such as depression and anxiety that lead to a reduction in the quality of life [2].

Hence, an appropriate diagnosis and accurate treatments against follicular degeneration are dermatological requirements to specifically target

the disease. Novel emerging therapies and new investigational drugs are regularly reported in the scientific literature. However, current available Food and Drug Administration (FDA)-approved options are limited to oral finasteride and topical minoxidil. Unfortunately, adverse effects and lack of persistence induce the noncompliance of patients, and therefore new therapeutic medications are needed to promote follicular growth and prevent hair loss[3].

Hair transplantation constitutes the backbone of hair replacement surgery. This technique, also known as follicular unit strip surgery (FUSS), was introduced in the mid-1990s and is based in a single elliptical strip excision of the posterior occipital area of the scalp followed by suture. The procedure harvests a great quantity of follicular units that are seeded back into the receptor area resulting in an effective treatment option for baldness[4].

However, the remaining linear scar stands as a major concern for patients especially in individuals with very tight scalp where primary closure is difficult. In the last few years, refinements in the technique have been developed with the introduction of individual follicular unit removal thanks to small punch excisions rather than single strip method. This minimally invasive surgery, also known as follicular unit extraction (FUE), is nowadays the gold standard of hair transplantation as excellent esthetic results are achieved with barely undetectable postoperative scar[5].

Platelet Rich Plasma (PRP) is based on the recovery of a small volume of the patient's own blood which is afterward centrifuged and activated to obtain an autologous formulation enriched in proteins and growth factors. The use of this approach enhances the patient's self-healing ability and promotes tissue renewal thus providing a therapeutic option for hair follicle regeneration [6]. The aim of the current study was to provide clinical evidence to support this hypothesis and evaluate the safety and efficacy of PRP in combination with FUE surgery for the treatment of androgenic alopecia.

## METHODS

This prospective comparative study included 16 patients with androgenetic alopecia. This study was performed during the period from January 2019 to January 2020 in the Plastic & Reconstructive Surgery Department of Zagazig University Hospitals. All these patients were divided, according to receiving platelet rich plasma (PRP) or not into two studied groups: Group (1); included eight patients treated with FUE with PRP; their age ranged between 22-40 years with mean of 32.50 years. Group (2); included eight patients treated with follicular unit extraction (FUE) without PRP; their age ranged between 24-43 years with mean of 33.17 years. Written Informed consent was taken from the patient to participate in the study. Approval for performing the study was obtained from Plastic & Reconstructive Surgery Department, Zagazig University Hospitals after taking Institutional Review Board (IRB) approval. Study has been carried out on experiments involving human subjects in compliance with the Code of Ethics of the World Medical Association (Declaration Helsinki).

**Inclusion criteria:** Male patients in the age group of 18–50 years. Patients with androgenetic alopecia (AGA) Stage III–VII Hamilton–Norwood classification. Patients who had not taken any form of treatment for AGA, at least in the past 3 months. **Exclusion criteria:** Patients on anticoagulant medications: aspirin, warfarin, heparin. Patients with alopecia other than AGA. Patients with

history of bleeding disorders, thyroid disease, autoimmune disorders, psoriasis or lichen planus. Patients with active infection or malignancies. Active viral hepatitis patients.

**Sample size:** Assuming that terminal hair follicle counts in  $1 \times 1 \text{ cm}^2$  patch area before intervention is  $28.9 \pm 5.0$ , 3 months after intervention is  $21.5 \pm 5.0$ , at confidence level 95%, power 80%, so total sample size is 16 patients. Calculated by open Epi.

### **Pre-operative:**

All patients underwent comprehensive history performed according to Hamilton–Norwood classification, Routine laboratory investigations performed according to Clinical Pathology Department Protocol in Zagazig University Hospital and it included; Complete blood picture (CBC) measured by automated blood counter. Liver function tests, Kidney function tests, Bleeding profile and Virology.

About 10 mL of blood was drawn from each patient in two sterile vacutainer tubes without anticoagulant and then the tubes were placed in a centrifuge at 3,000 revolutions per minute (rpm) for 10 minutes. After centrifugation, three layers were obtained; yellow-colored acellular plasma in the upper layer, red colored red blood cells (RBCs) in the lower layer, and PRP in the middle layer. The middle layer was used for applications in this study.

The subjects were treated with intradermal injections of autologous PRP two times; first 14 days prior to FUE, and the second 14 days after FUE. An equal number of follicular units was implanted in a  $1 \times 1 \text{ cm}^2$  area. Follicular density was measured using Trichoscope taken immediately, at three and six month follow up visits. Hair density indices were compared using Trichoscope with from similar areas as control on same subjects without PRP injections.

**Operative plan:** Only scalp hairs were harvested. Transaction rate during harvesting was 5–8%. While doing implantation, only the grafts with intact roots were implanted. The follicles were kept moist in chilled normal saline and stored inside refrigerator at  $2-8^\circ$  centigrade till implantation Figure 1, 2.

### **Clinical assessment**

Photographs were taken from each patient at 24 hours and after 1 week using a digital camera (Nikon D7000, Tokyo, Japan). Each patient was photographed with clinical and video microscopic images, keeping identity confidential and data were evaluated independently.

A survey was conducted to determine the patient satisfaction in terms of postoperative pain relief, scalp itching reduction and inflammation phase resolution.

**Efficacy evaluation criteria**

The evaluation was done by analysis of preoperative and postoperative of follicular unit extraction hair transplantation and throughout the time of wound healing and complication management if occurred up to 6 months by Patient satisfaction questionnaire, scalp redness, hair density, length, direction & texture by using Trichoscopy (DermLite® San Diego, California, USA) in the analysis at the end of 2 weeks, 4 weeks, 8 weeks, 3 months and 6 months Figure 4

**STATISTICAL ANALYSIS**

All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows (SPSS Inc.,

**Table (1): Demographic data of the studied subjects.**

Variable	PRP (N=8)	Non-PRP (N=8)	t / $\chi^2$	P
<b>Age (years)</b> Mean $\pm$ SD Median (range)	32.50 $\pm$ 8.45 30 (22-40)	33.17 $\pm$ 9.35 34 (24-43)	2.729	0.164 (NS)
<b>HTN</b>	3 (37.5%)	2 (25%)	2.616	0.197 (NS)
<b>Smoking</b>	2 (25%)	1 (12.5%)	3.111	0.211 (NS)
<b>Diabetes Mellitus</b>	1 (12.5%)	0 (0%)	1.091	0.296 (NS)

This study showed that regarding PRP group, 2 patients (25%) were grade III, 4 patients (50%) were grade IV, one patient (12.5%) was grade V and one patient (12.5%) was grade VI. Regarding PRP group, 3 patients (37.5%) were grade III, 2 patients (25%) were grade IV, 2 patients (25%) were grade V and one patient (12.5%) was grade VI table 2.

**Table (2): Hamilton-Norwood classification of alopecia between the two studied groups.**

Variable	PRP (N=8)	Non-PRP (N=8)	t / $\chi^2$	P
<b>Grade III</b>	2 (25%)	3 (37.5%)	1.23	.753 (NS)
<b>Grade IV</b>	4 (50%)	2 (25%)		
<b>Grade V</b>	1 (12.5%)	2 (25%)		
<b>Grade VI</b>	1 (12.5%)	1 (12.5%)		

This study showed that regarding PRP group there were 2 patients (25%) were excellent, 3 patients (37.5%) were good and 3 patients (37.5%) were fair. Regarding non-PRP group there were 3 patients (25%) were excellent, 4 patients (50%) were good and one patient (12.5%) was poor. There was no significant difference between the two groups regarding satisfaction table 3.

**Table (3): Satisfaction of the two studied groups**

	PRP group (N=8)		Non-PRP group (N=8)		$\chi^2$	P
	No.	%	No.	%		
Excellent	2	25%	3	37.5%	4.343	.227 (NS)
Good	3	37.5%	4	50%		
Fair	3	37.5%	0	0		
Poor	0	0%	1	12.5%		

This study showed that regarding PRP group all patients were good. Regarding non-PRP group there were 5 patients (62.5%) were good and 3 patients (37.5%) were poor. There was significant difference between the two groups regarding clinical evaluation table 4.

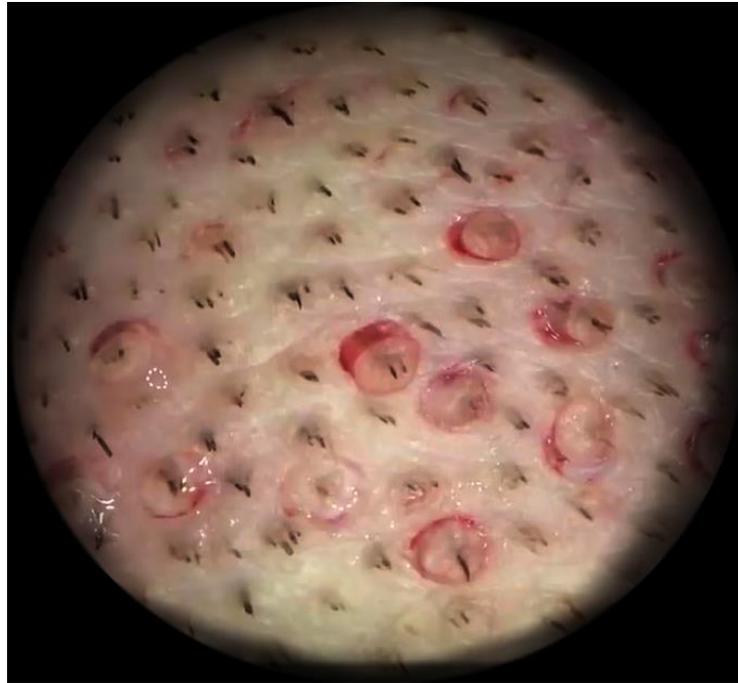
Chicago, IL, USA) & MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium)..

**RESULTS:**

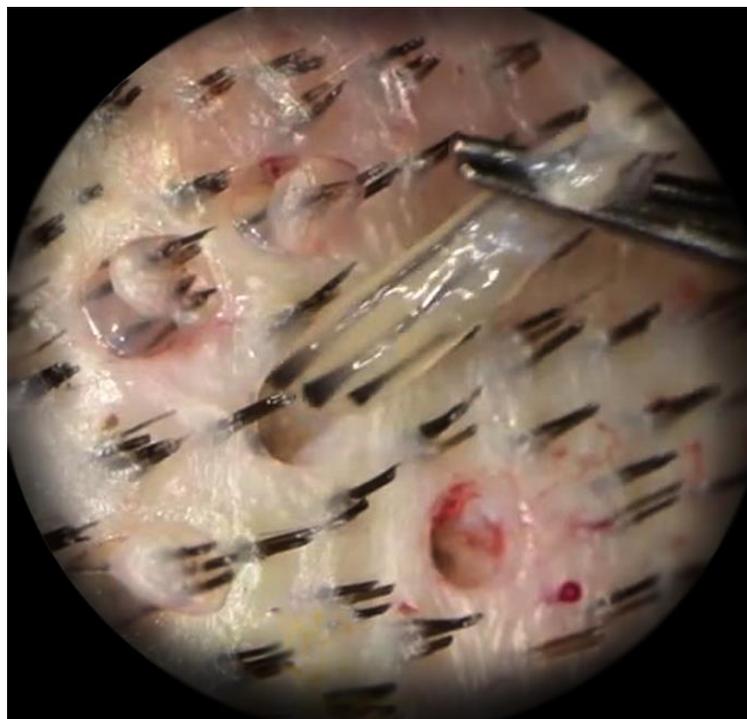
This study showed that the mean age of the patients treated with FUE with PRP was 32.50 $\pm$ 8.45 years, 3 patients (37.5%) were HTN, 1 patient (12.5%) was diabetic and 2 patients (25%) were smokers. The mean age of the patients treated with FUE without PRP was 33.17 $\pm$ 9.35 years, 2 (25%) were HTN and 1 patient (12.5%) was smokers. There was no significant difference found between the two groups table 1

**Table (4):** Clinical evaluation of outcome between the two studied groups

	PRP group (N=8)		Non-PRP group (N=8)		$\chi^2$	P
	No.	%	No.	%		
Good	8	100%	5	62.5%	<b>3.962</b>	<b>.045</b> (S)
Poor	0	0%	3	37.5%		



**Figure 1.** Tricoscopic picture after making punches



**Figure 2.** Tricoscopic picture while extracting follicle

The follicles were implanted within 6 h of harvesting in both the groups and the roots were not fiddled with while implantation. The density of implantation was kept at 40–45 grafts/cm<sup>2</sup> in both groups using multipronged slider Figure 3.

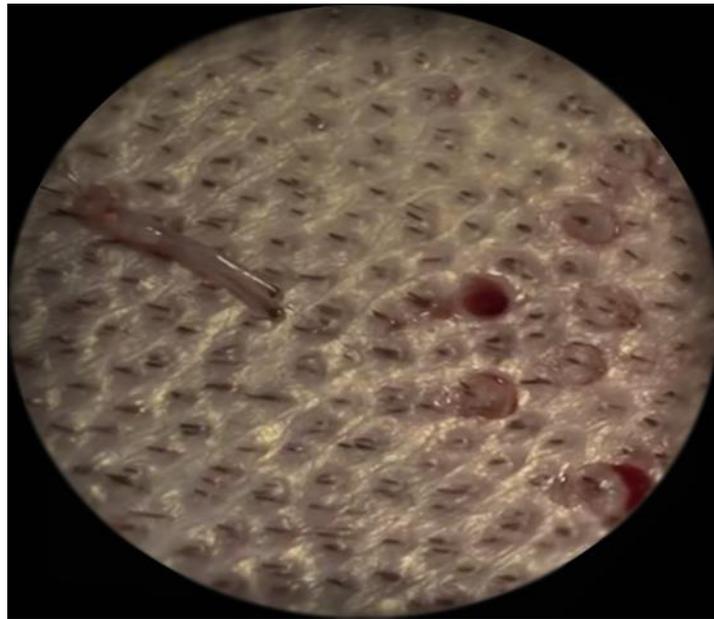


Figure 3. Tricoscopic picture of extracted follicle



Figure 4. Tricoscopic picture after follicles implantation

### DISCUSSION

In this study, we found that platelet rich plasma (PRP) showed a better outcome based on the clinical evaluation, that we found a significant difference between PRP group (in which all patients have a good outcome) and non-PRP group (only 62.5% of the patients have a good outcome). These findings were in line with Rastegar et al. [7], Navarro et al. [8].

In Garg, [9] study, all patients in PRP-treated group had more than 75% follicle growth whereas in non-PRP treated group only 20% of the patient showed

more than 75% follicle growth. They also reported that the quality of hair was better in PRP-treated group as compared to non-PRP group. In PRP group, multiple erupting roots from the graft as early as 3 months besides length of shafts clearly suggest the role of growth factors in PRP in stimulating as well as nourishing transplanted follicular unit grafts.

Moreover, these results are consistent with other studies that have highlighted the mitogenic potential of platelet-rich plasma over bulbar cells, by means of extracellular signal kinases/Akt

pathway activation and CDK4/cyclin D1 overexpression [7].

Uebel et al. [10] suggested that the catagen loss in transplanted hair reduced significantly at 1 month interval though there was a delayed fall but not as clear as in non-PRP group. The fall was noticed as breakage of hair strand just above skin surface rather than actual shedding of transplanted hair in these cases. This can be explained by the effect of growth factors on the newly transplanted hair. Furthermore, the new growth of follicles was noticed as early as 2 months in video microscopic images.

On the other hand Garg, [9] reported that in non-PRP group, 65% clients showed the length of follicles 6–10 mm at 6 months meaning most of these trailing follicles entered anagen phase more recently. The injected therapy could be better as there is less wastage, added benefit of faster recovery of skin, activity of dormant follicles and faster entry into the new anagen hair.

The combination of growth factors plays pivotal role in tissue repair, and regeneration and presence of plasma proteins act as a scaffold in epithelial migration. The effect may result into anagen hair growth as early as 2 months.

Navarro et al. [8] and Rahmani et al. [11] have shown that plasma rich in growth factors induces the bioactivation of two follicular cell phenotypes such as dermal papilla and germinal matrix cells. These cells are not only essential for hair development but behave also as a reservoir with the potential to differentiate and regenerate the multiple layers of the outgrowing shaft.

Navarro et al. [8] demonstrated that plasma rich in growth factors (PRGF) preservation increases the proliferative behavior of epidermal and bulbar cells even in hypoxic environment. Moreover, Tohidnezhad et al. [12] demonstrated that plasma rich in growth factors is able to reduce ROS levels after oxidative stress and activate detoxifying enzymes by the overexpression of the antioxidant response element (ARE) via Nrf2 nuclear factor upregulation.

Li et al. [13] reported that follicular cell death found to be significantly reduced after platelet-rich plasma treatment due to the activation of antiapoptotic regulators such as Bcl-2 protein thus stimulating hair growth.

Platelet Rich Plasma (PRP) is the source of various growth and regulatory factors involved in cells growth and differentiation. PRP not only induces growth but also improves cell survival by its anti-apoptotic activity. Activated PRP stimulates growth and differentiation of stem cells in hair follicle bulge along with activation of mesenchymal cells in dermal papilla. It stimulates

transcriptional activity of b-catenin responsible for differentiation of stems cells to hair follicle cells. PRP is reported to stimulate Bcl-2 regulatory protein levels, which possess anti-apoptotic activity and prolongs survival of derma papilla cells [9].

Platelet Rich Plasma (PRP) is also reported to activate Protein kinase B (AKT) and Extracellular signal-related kinase (ERK) signalling pathways to protective dermal papilla cells from apoptosis. PRP up-regulates FGF-7 growth factors, which are known to stimulate hair growth. VEGFs and platelet-derived growth factors contribute in increasing peri-follicular vasculature thus, improving the blood supply and nourishment to the transplanted grafts [14,15].

#### **Limitations:**

The study had some limitations including randomized clinical trials with higher number of patients and longer follow-up periods are needed to clarify the suitability of autologous growth factors for hair transplant treatment and to elucidate the underlying mechanisms by which PRP regulates tissue regeneration. More studies that compare between the two groups; half and half side of scalp rather than on different subjects.

#### **CONCLUSION**

This study demonstrated that PRP treatment during the hair transplant plays a significant role in hair regrowth, and it remarkably improves density and quality of hair growth. Finding the optimal therapeutic protocol appears to be a worthwhile pursuit when invasive surgical techniques like FUE are routinely performed. However, these preliminary findings suggest that PRP might offer a safe and effective adjuvant therapy for patients undergoing FUE surgery against alopecia.

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