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Follicular Unit Extraction with or without Platelet Rich Plasma in the Treatment of and Rogenetic Alopecia

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Abstract--- Background: *Androgenetic alopecia (AGA) is a genetically determined phenomenon that is defined by gradual loss and reduction of normal thick hair follicles. This study aimed to determine if Platelet Rich Plasma (PRP) assists in Follicular Unit Extraction (FUE) or not.* ***Patients and methods:*** *This is a prospective comparative study that was performed in the period from January 2019 to January 2020 in Plastic & Reconstructive Surgery Department of Zagazig University Hospitals. This study included 16 patients with androgenic alopecia checked at Plastic Surgery Outpatient Clinic, Zagazig University Hospitals. Patients included in the study was divided into two groups according to receiving RPR or not, Group (1); 8 Patients treated with FUE with PRP. Group (2); 8 Patients treated with FUE without PRP.* ***Results:*** *All 8 patients treated with PRP showed a good hair regrowth, with prefect outcome. Of the 8 patients treated without PRP, 5 showed a good hair regrowth, with good outcome.* ***Conclusion:*** *These preliminary findings suggest that PRP might offer a safe and effective adjuvant therapy for patients undergoing FUE surgery against alopecia.*

Keywords--- *Follicular Unit Extraction (FUE), Platelet Rich Plasma (PRP), Androgenetic Alopecia (AGA).*

I. INTRODUCTION

Male androgenic alopecia is one of the most prevalent dermal disorders in males. It is also referred to as male pattern baldness as it happens in specific pattern and it impacts adolescents as well as adults. Polygenic heredity is considered to be its cause; in addition, male hormone testosterone plays a major role[1].

Patients suffering from severe degree of hair loss-related disorders such as androgenetic alopecia are usually candidates for follicular unit extraction surgery [2].

Platelet Rich Plasma (PRP) is based on the recovery of a small volume of the patient's own blood which is

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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[3].

PRP is rich in many growth factors and proteins. It is very rich in PDGF, epidermal growth factor, transforming growth factor, fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF) and various pro and anti-inflammatory cytokines such as interleukin 4 (IL-4), IL-8, IL-13, IL-17, tumour necrosis factor alpha and interferon alpha. These growth factors may induce an internal signal-transduction pathway, unlocking the expression of a normal gene sequence of a cell thereby initiating and improving tissue regeneration process[4].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.

II. PATIENTS AND METHODS

Included 16 patients with androgenic alopecia checked, patients included in the study was divided into two groups according to receiving RPR or not, Group (1); 8 Patients treated with FUE with PRP. Group (2); 8 Patients treated with FUE without PRP. The average age and degree of medical comorbidities were comparable in the 2 groups. Written informed consent was obtained from all participants and the study was accepted by the Research Ethics Committee of the Faculty of Medicine, Zagazig University.

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.

Pre-operative

All patients underwent comprehensive history includes name, age, sex, associated medical diseases 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; serum bilirubin (total and direct), serum albumin, serum alanine transaminase and aspartate transferase measured by kinetic method. Kidney function tests; serum creatinine, serum urea and serum uric acid by colorimetric assay. Bleeding profile; PT, PTT and INR. 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 1×1cm2 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

All the patients were given detailed pre- and post-operative instructions. 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° centigrade till implantation. 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/cm2 in both groups using multipronged slitter.

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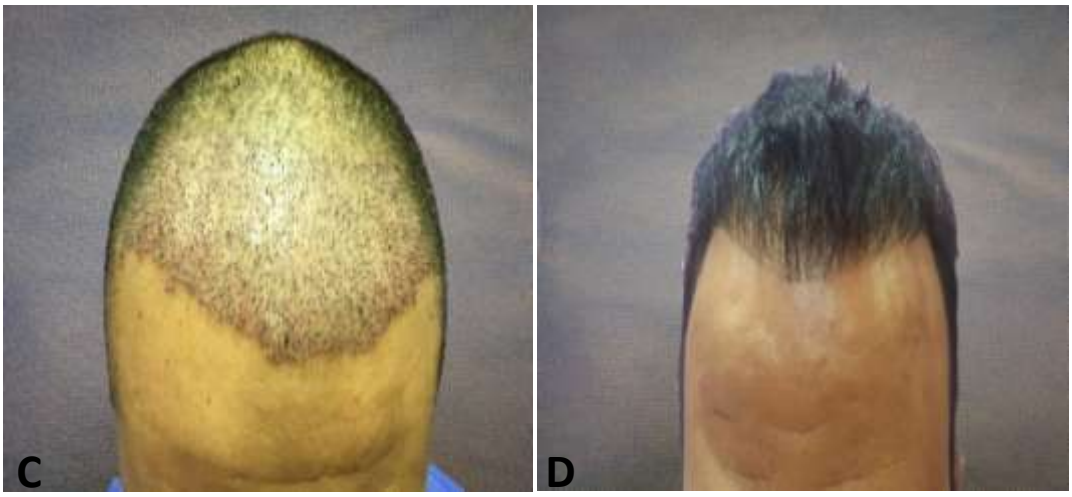
(A) Pre-operative (B) After Grafts Insertion

Post-operative

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.



(C) 3 Months Post-operative (D) 6 Months Post-operative

III. STATISTICAL ANALYSIS

All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows (SPSS Inc., Chicago, IL, USA) & MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium).Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean ± SD (Standard deviation) for parametric and median and range

for non-parametric data. Independent T test and Mann- Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively. Level of P-value ≤ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates Non-significant difference.

IV. RESULTS

This study showed that the mean age of the patients treated with FUE with PRP was 32.50±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±9.35 years, 2 (25%) were HTN and1 patient (12.5%) was smokers. There was no significant difference found between the two groups table 1.

Table 1: Demographic Data of the Studied Subjects.

Variable	PRP (N=8)	Non-PRP (N=8)	t / χ^2	P
Age (years) Mean ± SD Median (range)	32.50 ± 8.45 30 (22-40)	33.17 ± 9.35 34 (24-43)	2.729	0.164 (NS)
HTN	3 (37.5%)	2 (25%)	2.616	0.197 (NS)
Smoking	2 (25%)	1 (12.5%)	3.111	0.211 (NS)
Diabetes Mellitus	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 / χ^2	P
Grade III	2 (25%)	3 (37.5%)	1.23	.753 (NS)
Grade IV	4 (50%)	2 (25%)		
Grade V	1 (12.5%)	2 (25%)		
Grade VI	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 Figure 1.

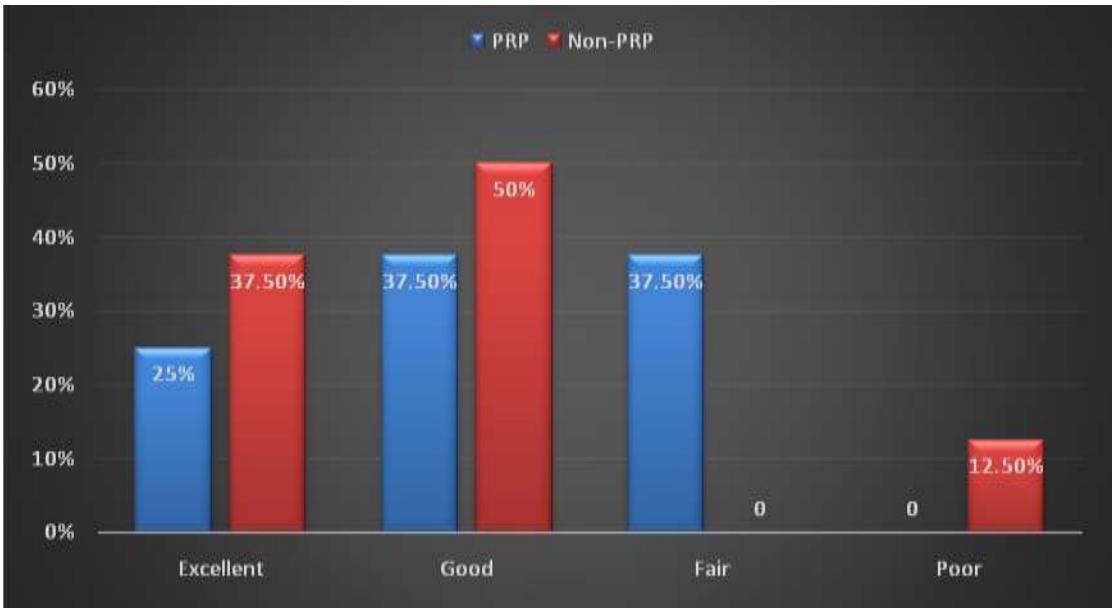


Fig. 1: Satisfaction of the Two Studied Groups

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 Figure 2.

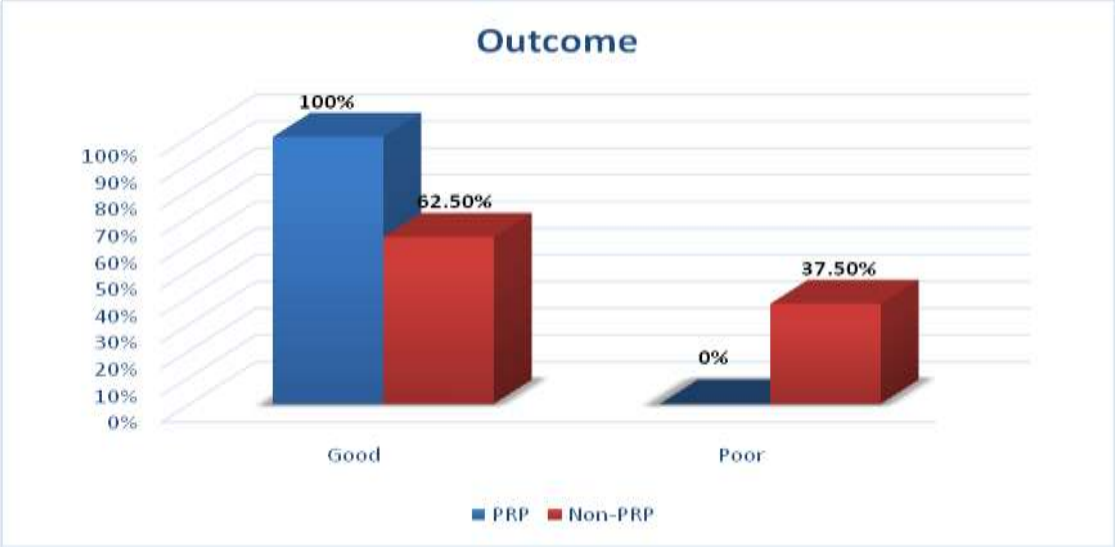


Fig. 2: Outcome Distributions between Patients

V. DISCUSSION

In this study, we found that 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.*** [5] and ***Navarro et al.*** [2].

In ***Garg,***[6]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 over expression [5].

Uebel et al.[7] suggested that the catagen loss in transplanted hair reduced significantly at 1 month interval though there was a delayed fall but not as severe 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.

Uebel et al.[7] reported that new anagen hair started after 4 months of transplant.

On the other hand ***Garg,*** [6] 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. [2] ***and Rahmaniet al.*** [8]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. [2]demonstrated that PRGF preservation increases the proliferative behavior of epidermal and bulbar cells even in hypoxic environment. Moreover, ***Tohidnezhad et al.***[9]demonstrated that plasma rich in growth factors is able to reduce ROS levels after oxidative stress and activate detoxifying enzymes by the over expression of the antioxidant response element (ARE) via Nrf2 nuclear factor upregulation.

Li, et al.[10] 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.

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 [3].

PRP is also reported to activate AKT and 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 [11,12].

VI. CONCLUSION

Platelet Rich Plasma (PRP) therapy improves the skin milieu of grafted area by cell growth and differentiation, anti-apoptotic activity and neovascularisation making grafted area more receptive and fertile for newly transplanted hair. It also helps in providing conducive environment for dormant hair follicles leading to their activity and appearance of new anagen hair as early as 2 months.

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