



# Efficacy Of Photobiomodulation Versus Its Combination with Plasma Rich Growth Factors or Minoxidil in Management of Androgenetic Alopecia

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## Abstract

**Background:** Androgenetic alopecia (AGA) is considered the utmost familiar etiology of hair loss in males. Topical minoxidil and more recently low-level light therapy (LLLT) or photobiomodulation in addition to plasma rich growth factors (PRGFs) known also as platelets rich plasma (PRP) therapy have been used in the management of AGA.

**Objectives:** To evaluate which is more effective for the management of androgenetic alopecia: LLLT alone, LLLT with PRGFs or with topical minoxidil.

**Materials and methods:** Forty-five patients having androgenetic alopecia were divided randomly into 3 equal groups: (Group A) were subjected to PRP therapy plus LLLT, (Group B) were subjected to minoxidil therapy plus LLLT and (Group C) were subjected to LLLT alone. All groups were treated for 3 months and were followed up for another 3 months after stopping treatment. Efficacy was assessed using global photography, follicoscopic pictures analysis and patient satisfaction score after a standardized hair growth inquiry form.

**Results:** By the end of the sixth month, (Group A) was found to have the best statistically significant improvement followed by (Group B) then (Group C). This was clearly obvious in global photography, follicoscopic analysis, and patient's satisfaction.

**Conclusion:** Combination of PRP with LLLT is better than its combination with minoxidil or as monotherapy in the management of AGA.

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**KeyWords:** androgenetic alopecia, Platelets-rich plasma, Minoxidil, Low-level laser therapy

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## Introduction

Androgenetic Alopecia is considered the most prevalent type of alopecia with special patterns in males and females. The pathogenesis comprises androgen mediated process known as miniaturization in which there is variation in dynamics of hair cycle resulting into a spectral & gradual transformation of hair from terminal to intermediate to vellus ones (1-3). Because it is a common disorder and the treatment options are limited, it is considered as an increasing

apprehension for dermatologists globally. Food and Drug Administration (FDA) accepted oral finasteride and topical minoxidil as medical treating options for managing AGA (4). Both drugs generally provide good results. On the other hand, patients with a weak response or experiencing side effects look for additional or alternative treatment options, such as LLLT which have been utilized as a substitute or as adjuvant in management of AGA.

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In general, LLLT uses the non-heating properties of red/near-infrared wavelengths at low powers where it exerts a photobiomodulation or a photobiostimulation effect. Also (5), PRP or PRGFs are considered a quite novel modality showing promising results in hair loss. It includes a preparation of platelets derived from the same individual into a less plasma volume containing over than twenty growth factors (GFs) through these GFs, PRP enhances hair growth in AGA by numerous ways (6). This current research targeted the evaluation of the clinical usefulness of LLLT usage when combined with PRP and whether this combination is more efficacious if we use LLLT alone or when combined with minoxidil solution.

### Material And Methods

The present randomized medical study was accomplished in the dermatologic out-patient treatment center in the National Institute of Laser Enhanced Sciences (NILES), Cairo University, Egypt. Approval of the dermatologic Researching Ethical Board was obtained from NILES, Cairo University. Moreover, we obtained informed written signed consent explaining the benefits and side effects, from every patient. Forty-five adult male patients aged more than eighteen years suffering from grade II-IV AGA as described by the classification scale of Norwood-Hamilton (7) were enrolled in this study. Patients were excluded if there was any other reason for hair loss such as thyroid dysfunction, bad nutrition, anemia or systemic evidence of platelet disorders, uncontrolled diabetes, immunosuppression, sepsis and cancer, or the use of oral or topical therapeutics targeting AGA in the previous 12 months. Patients were asked about smoking or any factor such as ultraviolet exposure which can aggravate AGA. Diagnosis of AGA was proven on the base of a meticulous medical record, proper clinical inspection, and trichoscopic features. The diameter and density of hair were accurately and objectively measured using a Folliscope (Compare view, ver. 1.5.09, CA-USA). An area of about  $14\text{mm}^2$  zone of the scalp was demarcated for each patient and was the same to be investigated pre, post treatment and at follow up. Hair density was calculated by counting the number of hairs in this zone. Hair width or diameter was found after the calculation of the average value of the width of 5 hairs which were randomly chosen in that zone. Also terminal to vellus ratio was measured.

### Protocol of treatment

All included patients were subdivided randomly into 3 equal sets group 15/each by using the envelope concealment manner. Patients belonging to (group A) were treated by 4 sessions of PRP injections combined with sessions of LLLT, (Group B) patients were notified to rub the affected area with 1ml of 5% minoxidil solution topically (6 puffs) twice daily for 3 months combined with sessions of LLLT, (Group C) patients had only received sessions of LLLT. In this present study, PRP had been prepared by the same means Verma and colleagues did in the form of manual double-spin technique. About 25–35 ml of venous blood was drawn into a tube-containing anticoagulant sodium citrate, to avoid platelets activation and degranulation. Blood was processed for the first centrifugation at approximately 1500 rpm for 5 min, which separated blood into three layers. Using a sterile syringe PPP, PRP and some RBCs were transferred into another tube without an anticoagulant. This tube underwent a second centrifugation at around 2500 rpm for 15 min. The PRP formed was collected into an insulin syringe, already containing calcium gluconate which acted as an activator by nullifying action of anticoagulant. Ratio of calcium gluconate and PRP in insulin syringe was 1:9. PRP thus formed was injected intradermally in a dose of 0.1–0.2 ml per injection approximately 1 cm apart in interfollicular areas (8). The protocol of LLLT was the same for all the forty five patients as twenty five minutes duration with the iGROW1 cap/helmet apparatus. This device has twenty-one laser diodes and thirty Light emitting diodes (LEDs) that can emit 655 nm red laser and outputting less than 5mW in a continuous wave (CW). The LED's wavelength ranged from 650 up to 670 nm. Sessions were performed three times per week not on consecutive days for three months. All patients were followed up for another three months after cessation of treatment.

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### Hair Growth Parameters Assessment

All AGA patients were evaluated upon their initial visit, at 3 and 6 months from the start of the treatment through Global clinical photography, patient's satisfaction and objectively by folliscope assessing the hair measures (hair density, terminal/vellus ratio and hair diameter). Patient satisfaction degree was described as: very satisfied, satisfied, neutral and dissatisfied. The



occurrences of unwanted reactions if any were stated

### Statistical Analysis

All information and data were collected, put in tables then analyzed statistically by means of SPSS20.0 version for window (SPSS Inc., Chicago, IL, USA). Expression of quantitative information as means  $\pm$ SD was done. Comparisons between the three groups were completed by using one way ANOVA for variables that are typically dispersed. Posthoc tests were performed to compare between each two groups. Repeated measurement ANOVA was done to do comparisons among measurements of variables that are normally distributed at different intervals within the same group. Also, paired t test was done to compare each 2 measurements. Expression of qualitative data as absolute frequencies (numbers) & relative frequencies (percentages) was done. Chi-square test was used to compare the percentage of categorical elements. Totally tests were two sided. P-values  $\leq$  0.05 were estimated as statistically remarkable and significant (S). On the other hand, P-values  $>$  0.05 were estimated as statistically unimportant and insignificant (NS).

### Results

This study included 45 adult male patients with confirmed AGA. These were divided haphazardly into three equivalent (fifteen/each): A, B and C. The Mean  $\pm$  SD age of patients in groups A, B and C was as (30.46 $\pm$ 3.94), (31.93 $\pm$ 3.69) and (32.60 $\pm$ 3.97) years respectively. Twenty patients were classified as grade II, 21 patients as grade. III and 4 patients as grade IV.

Demographic data as well as clinical ones didn't show any significant alteration or difference between the 3 groups. Also, no statistically significant difference existed between the three groups as  $p > 0.05$  on the subject of follisopic pretreatment hair measures: density, terminal/vellus hair ratio and diameter. Regarding follisopic hair measures of (Group A) and (Group B), we found a statistically significant improvement of pretreatment terminal hair diameters plus densities in comparison with results three months after end of sessions. At Follow up and after stoppage of treatment by three months, statistically significant decrease was noticed in hair density and terminal hair but still significantly better than pretreatment results as shown in tables 1 & 2. While for (Group C) where  $P \geq 0.05$ , no statistically

significant change was found between pretreatment results of hair density, terminal hair and hair diameter and results following treatment and those after its stoppage as shown in table 3. By comparing the follisopic findings among the different groups following three months of treatment and at three months after its stoppage, there was a statistically significant difference ( $P < 0.05$ ) among the three groups regarding hair measures [density, terminal /vellus hair ratio and diameter]. (Group A) showed the best improvement followed by (Group B) then (Group C), as shown in tables 4& 5 (Fig.1&2). This follisopic result was corresponding to the comparison between the three groups as regards the global photography as shown in fig.3. These previous results were matching with a significant alteration that was observed between the 3 groups as regarding the level of satisfaction of patients with the highest grade of satisfaction found in (Group A) followed by (Group B) then (Group C) as shown in table 6.

As regard the side effects among (Group A), 2 patients complained of headache and pain which occurred at the sites of PRP injection. It was tolerable and temporary. Two patients complained of transient edema. Among (Group B), 3 patients reported mild headache while 4 patients complained of scalp tenderness. Thirty six out of 45 patients complained of warm sensation during the LLLT session. All symptoms were mild and lasted only several minutes after the session.

### Discussion

Androgenetic alopecia in men is a continuous hair loss with a special pattern in which susceptible terminal hair is converted into vellus like hair in genetically predisposed individuals. This conversion is androgen mediated (8). LLLT is considered a somewhat novel FDA accepted method with promising efficiency in enhancing growth of hairs in both men and women with AGA (9). There are many postulated modes of operations. The chief mode is that LLLT stimulates epidermal stem cells in the bulge of follicles and motivates them to change into the anagen stage (5,10). The minority of medical studies considering the combined modalities directed us to evaluate and compare the clinical efficacy of LLLT combined with PRP versus LLLT alone and versus its association with topical minoxidil 5% solution for treatment of this challenging condition. The three

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modalities showed variable degree of clinical improvement based on objective evaluation using the folliscope together with patients' satisfaction. The combined PRP and LLLT showed significant better outcomes when compared to pre-treatment, afterwards, and follow-up period and also when compared with those of the combined Minoxidil and LLLT or with LLLT alone.

These significant results could be due to the anti-apoptotic effects that has been proposed to be a very important factor that stimulates hair growing through Bcl-2 protein activation which is an anti-apoptotic regulator and thus upgrading the longevity of the cells present in the dermal papilla (DPCs) (11-14). Moreover, the up regulation of fibroblast growth factor-7 (FGF-7) or b-catenin signaling pathway with PRP treatment have been hypothesized to enhance hair growth by prompting hair follicle stem cells (HFSC) differentiations and prolongation of the anagen phases of the hair growth cycles (11-14). It also appears to enhance the vascular plexuses around the follicles through the rise of platelet-derived growth factors (PDGF) level in addition to vascular endothelial growth factors (VEGF), which have angiogenic effects (11-14). This improvement is clearly obvious in the global photography and objectively in images of the folliscope that disclosed higher significant increases in hair densities and diameters 3months after treatment and also at three months after cessation of treatment than the other two groups. Gentile and his colleagues investigated 23 patients with AGA (13 male +10 female) treated with LLLT represented by helmet Hair Gentron® (DTS MG Co., Ltd., Seoul, Korea, #B108-147), two times per week for 24 weeks combined with ANA-PRP 3 sessions 30 days apart, plus micro needling technique (MN-T) just before each PRP infiltration and repeated every 15 days for 3 times (15). In spite of the difference between Gentile 's study and this current study as regards the technique of PRP preparation, because they used autologous non-activated formula of PRP (ANA-PRP) which differs from the activated formula which was used in this current study and moreover they used MN-T which is postulated to enhance the vascularity of the areas to be injected with ANA-PRP and, at the identical period, defining follicles disruptions generating GFs and collagen (16), both studies are in agreement in that combination of LLLT with PRP is a good and safe modality in the management of AGA .

Also, the improvement of group B (LLLT plus minoxidil 5% topical solution) was better than that

of group C (LLLT only) and this was in agreement with Esmat and colleagues who investigated forty five females with FPHL (17). Patients were divided randomly into 3 equal groups, where group (A) patients applied 5% minoxidil topically twice per day, group (B) patients were exposed to LLLT sessions with the helmet iGrow1 device for twenty-five minutes three days weekly & group (C) the combined group as patients applied 5% minoxidil topically twice per day with LLLT for twenty five minutes three days per week for four months (the clinical trial length). They evaluated their patients clinically; by dermoscopic (folliscope) examination and US bio microscopic measurements (UBM). They concluded that combination of LLLT plus minoxidil 5% topical solution was better than LLLT as a monotherapy. Minoxidil efficacy could be due to its ability to augment blood flow of the skin and increase vascular endothelial growth factor as well as other promoters for hair growth in the dermal papillae (18). It also stimulates cellular proliferations, increases angiogenesis, and DNA production (19). In addition, it can increase hair growth by increased prostaglandin E2 production via stimulation of Pendoperoxidase-1 (20). Moreover, minoxidil can extend the anagen phase, reduce the telogen phases and increase the sizes of follicles that has been shrunken (20). An initial increase of hair shedding was reported in our group B as a side effect to minoxidil (21). This shedding improved within a few weeks with continuance of the use of minoxidil and this may explain the upper hand results of PRP. Based on previous experiences, LLLT of 650 nm up to 900 nm wavelength at five mwatts has been proposed to be an efficacious choice for patients in case of male or female pattern hair loss. That's why we used the iGROW1 cap or helmet device with twenty-one laser diodes and thirty LEDs, red laser 655 nm with a CW output <5mW. LED wavelength ranged from 650 to 670nm in this current study. Though specific studies assessing laser modalities are lacking, LLLT has been suggested to speed up cell division and mitosis, to enhance stem cells of the hair follicle and to activate follicular keratinocytes. Moreover, resolving inflammation may be one possible mechanism of hair growth stimulated by LLLT in AGA (22). Despite of all these postulated mechanisms in treatment of AGA, the improvement in the appearance of hair overall and the decrease in hair fall which was noticed by some patients and recorded by the folliscope (as increase in hair



density when comparing the pre and the post treatments measures of hairs in group C), the difference was not statistically significant, and this was in agreement with Avram & Rogers, who considered the usage of LLLT for treatment of hair loss in 7 patients (six females & one male) (23). Their results for vellus/terminal hair, shaft diameter and hair count were statistically insignificant.

In spite of this, we are sharing with other researchers the view that LLLT has the potentiality of being an effective treatment and promising safe one especially when combined with PRP or with minoxidil solution, as this combination may act synergistically thus enhancing the growth of hair. This may explain the significant and better improvement results of group A and group B when matched with group C in this current experiment. We may hypothesize that improvement effect is mainly due to PRP and minoxidil solution as in Verma and colleagues who studied 30 patients who were randomly divided into 2 groups, group A received PRP treatment every month and group B received minoxidil therapy 1 ml twice daily for 6 months. At the end of 6 months, group A had better outcome than group B. All the modalities used were

safe and we did not detect any serious side effects in any of the included patients, unless self-limited mild degree of irritation and scalp tenderness, especially among group B patients. This was described before by Rossi A ,et al with minoxidil treatment (18). The warm sensation with most of patients after LLLT session was stated by Jimenez and his colleagues as it may be due to an increase in the blood flow and the induction of vasodilation as an effect of LLLT (22,24). As regards PRP treatment we reported tolerable and temporary pain, mild headache during treatment, desquamation , and mild itching as well as temporary edema as described by Cervantes and coworkers (25).

**Conclusions & Recommendations**

Finally, we can conclude that combination techniques of LLLT with PRP or with minoxidil as a management of AGA is better than LLLT alone and patients may benefit from more than one mechanism of action. LLLT combined with PRP gives better improvement than with minoxidil but for further studies with increased number of patients, different protocols and longer follow up durations.

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**Table 1: Comparing different hair parameters at different intervals in group A**

Variables	Pre Treatment	After Treatment	Follow Up	P value
Density: Mean± SD (min-max)	110.24±15.35 (91.1-143.1)	138.8±11.71 (120.4-166)	130.45±14.2 (110.7-159.5)	0.121 P1<0.001 P2<0.001 P3<0.001
Terminal hair: Mean± SD (min-max)	71.08±9.1 (51.6-87.5)	85.70±4.96 (80.4-95)	81.06±4.86 (73.5-90.0)	0.002 P1<0.001 P2<0.001 P3=0.002
Vellus hair: Mean± SD (min-max)	28.92±9.11 (12.5-48.4)	14.30±4.96 (5-19.6)	18.94±14.2 (10-26.5)	0.002 P1<0.001 P2<0.001 P3=0.001
Diameter: Mean± SD (min-max)	0.077±0.008 (0.06-0.09)	0.096±0.007 (0.09-0.11)	0.094±0.007 (0.08-0.11)	0.08 P1<0.001 P2<0.001 P3=0.189

Repeated measurement ANOVA Test with paired t test for each two intervals P1 between before treatment results and results after 3 months

P2 between before treatment results and 3 months after stoppage of treatment P3 between after treatment results and 3 months after stoppage of



treatment

**Table 2: Comparing different hair parameters at different intervals in group B (minoxidil group)**

Variables	Pre Treatment	After Treatment	Follow Up	P value
Density: Mean± SD (min-max)	112.85±13.82 (94.4-136.7)	127.9±12.01 (110.7-149)	118.46±12.16 (109-140)	0.78 P1<0.001 P2<0.001
Terminal hair: Mean± SD (min-max)	69.62±6.27 (55-78.1)	81.79±6.21 (68.2-89.2)	76.04±6.58 (62.5-87.5)	0.06 P1<0.001 P2<0.001 P3=0.002
Vellus hair: Mean± SD (min-max)	30.39±6.27 (21.9-45.0)	19.21±6.21 (10.8-31.8)	23.69±12.16 (12.5-37.5)	0.06 P1<0.001 P2<0.001 P3=0.002
Diameter: Mean± SD (min-max)	0.075±0.01 (0.06-0.09)	0.09±0.009 (0.08-0.11)	0.086±0.009 (0.07-0.1)	0.024 P1<0.001 P2=0.001 P3=0.05

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Repeated measurement ANOVA Test with paired t test for each two intervals  
 P1 between before treatment results and results after 3 months  
 P2 between before treatment results and 3 months after stoppage of treatment  
 P3 between after treatment results and 3 months after stoppage of treatment

**Table 3: Comparing different hair parameters at different intervals in group C**

Variables	Pre Treatment	After Treatment	Follow Up	P value
Density: Mean± SD (min-max)	109.5±15.8 (92.5-143.2)	109.38±15.41 (91.1-140)	108.5±11.5 (91.1-130.2)	0.98 P1=0.99 P2=0.694 P3=0.695
Terminal hair: Mean± SD (min-max)	69.04±6.86 (53.3-76.5)	68.99±6.59 (53.3-76.5)	70.16±4.61 (60-78.6)	0.001 P1=0.084 P2=0.315 P3=0.552
Vellus hair: Mean± SD (min-max)	30.96±6.87 (23.5-46.7)	30.99±6.59 (22.1-46.6)	29.84±11.5 (21.4-45.0)	0.001 P1=0.084 P2=0.315 P3=0.552



Diameter: Mean± SD (min-max)	0.072±0.007 (0.06-0.08)	0.076±0.008 (0.06-0.1)	0.077±0.006 (0.07-0.09)	0.501 P1=0.02 P2=0.03 P3=0.719
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Repeated measurement ANOVA Test with paired t test for each two intervals  
 P1 between before treatment results and results after 3 months  
 P2 between before treatment results and 3 months after stoppage of treatment  
 P3 between after treatment results and 3 months after stoppage of treatment

**Table 4: Comparing different hair measures between the three groups at 3 months of treatment (n=45).**

Variables	Group A (n=15)	Group B (n=15)	Group C (n=15)	F	P value
Density: Mean± SD (min-max)	138.8±11.71 (120.4-166)	127.9±12.01 (110.7-149)	109.38±15.41 (91.1-140)	19.2.	<0.001 P1=0.028 P2<0.001 P3<0.001
Terminal hair: Mean± SD (min-max)	85.70±4.96 (80.4-95)	81.79±6.21 (68.2-89.2)	68.99±6.59 (53.3-76.5)	19.2.	<0.001 P1=0.029 P2<0.001 P3<0.001
Vellus hair: Mean± SD (min-max)	14.30±4.96 (5-19.6)	19.21±6.21 (10.8-31.8)	30.99±6.59 (22.2-46.7)	27.77	<0.001 P1=0.029 P2<0.001 P3<0.001
Diameter: Mean± SD (min-max)	0.096±0.007 (0.09-0.11)	0.09±0.009 (0.08-0.11)	0.076±0.008 (0.06-0.09)	21.32	<0.001 P1=0.05 P2<0.001 P3<0.001

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One way ANOVA Test with post hoc test P1 relation between groups A and B  
 P 2 relation between groups A and C P 3 relation between groups B and C

**Table 5: Comparing different hair parameters between the studied groups 3 months after stoppage of treatment (n=45).**

Variables	Group A (n=15)	Group B (n=15)	Group C (n=15)	Test	P value
Density: Mean± SD (min-max)	130.45±14.2 (110.7-159.5)	118.46±12.16 (109-140)	108.5±11.5 (91.1-130.2)	11.27	<0.001 P1=0.013 P2<0.001 P3=0.037
Terminal hair: Mean± SD (min-max)	81.06±4.86 (73.5-90.0)	76.04±6.58 (62.5-87.5)	70.16±4.61 (60-78.6)	15.49	<0.001 P1=0.04



					P2<0.001 P3=0.001
Vellus hair: Mean± SD (min-max)	18.94±14.2 (10-26.5)	23.69±12.16 (12.5-37.5)	29.84±11.5 (21.4-40.0)	15.46	<0.001 P1=0.04 P2<0.001 P3=0.001
Diameter: Mean± SD (min-max)	0.094±0.007 (0.08-0.11)	0.086±0.009 (0.07-0.1)	0.077±0.006 (0.07-0.09)	16.75	<0.001 P1=0.008 P2<0.001 P3=0.004

One way ANOVA Test with post hoc test P1 relation between groups A and B P 2 relation between groups A and C P 3 relation between groups B and C

**Table 6: Comparing satisfaction with treatment and effectiveness of the treatment between the studied participants (n=45).**

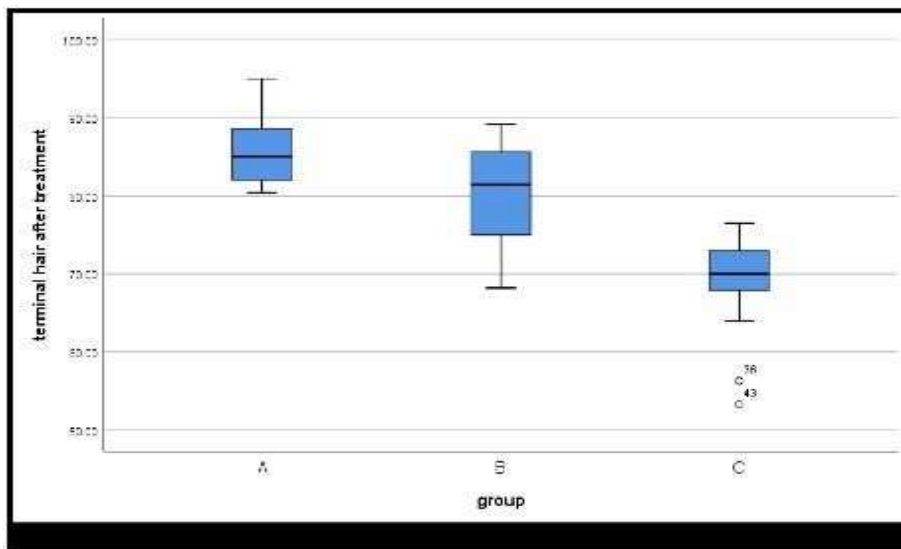
Variables	Items	Group A (n=15)		Group B (n=15)		Group C (n=15)		P value
		N	%	N	%	N	%	
satisfaction with the appearance of hair overall	Dissatisfied	2	13.3	5	33.3	8	53.3	0.04*
	Neutral	2	16.7	5	41.7	5	41.7	
	Satisfied	7	35.8	4	30.8	2	15.4	
	Very satisfied	4	80.0	1	20.0	0	0.0	
satisfaction with the appearance of the top of hair	Dissatisfied	2	13.3	5	43.3	8	53.3	0.014*
	Neutral	2	14.2	6	42.9	6	42.9	
	Satisfied	8	66.7	3	25.0	1	8.3	
	Very satisfied	3	75.0	1	25.0	0	0.0	
satisfaction with the appearance of the front of hair	Dissatisfied	2	13.3	5	43.3	8	53.3	0.036*
	Neutral	3	21.4	5	35.7	6	42.9	
	Satisfied	7	58.3	4	33.4	1	8.3	
	Very satisfied	3	75.0	1	25.0	0	0.0	
How effective do you think the treatment has been in slowing down your hair loss?	Not effective	3	14.3	8	38.1	10	47.6	0.013*
	Somewhat effective	6	35.3	6	35.3	5	29.4	
	Very effective	6	85.7	1	14.3	0	0.0	
Describe the growth of your hair	No change	0	0.0	0	0.0	4	100.0	0.006*
	Slightly increased	2	13.3	6	40.0	7	46.7	
	Moderately increased	9	42.9	8	38.1	4	19.0	
	Greatly increased	4	80.0	1	20.0	0	0.0	





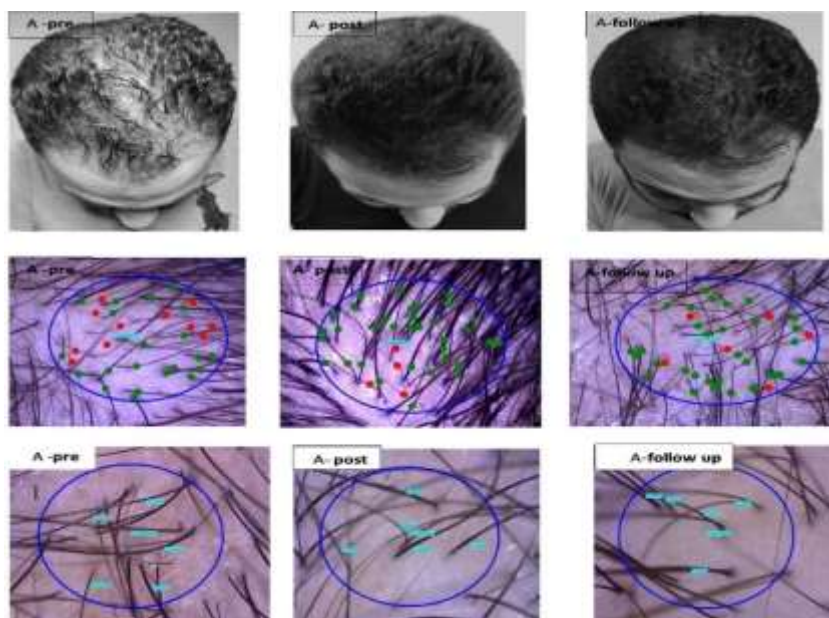
Since the start of the study , I can see my bald spot getting smaller	Strongly disagree	0	0.0	0	0.0	4	100.0	0.015*
	Disagree	2	20.0	4	40.0	4	40.0	
	Neutral Agree	2	15.4	6	42.2	5	38.5	
	Strongly agree	7	53.8	4	30.8	2	15.4	
		4	80.0	1	20.0	0	0.0	

Chi square test (X2)



**Fig 1: Comparing Terminal hair results after treatment between the three groups showing significant difference with best results in group A followed by B then C.**

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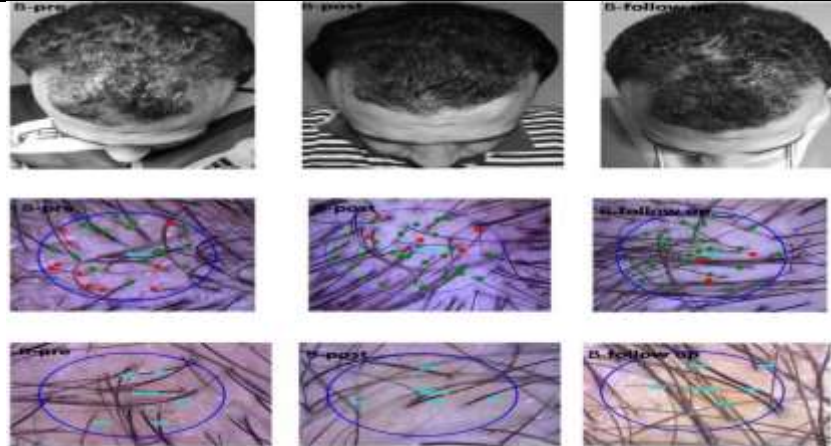


**Fig 2: Clinical and Folliscope Images (20x, 50x) of a patient of Group A and numbers of his Terminal & Intermediate Terminal and Vellus hairs in addition to the mean hair shaft diameter**

A-pre	104.2/cm <sup>2</sup> Terminal= 21Intermediate= 11Total= 32%T= 65.6%%I= 34.4%
A-post	123.7/cm <sup>2</sup> Terminal= 34Intermediate= 4Total= 38%T= 89.5%%I= 10.5%



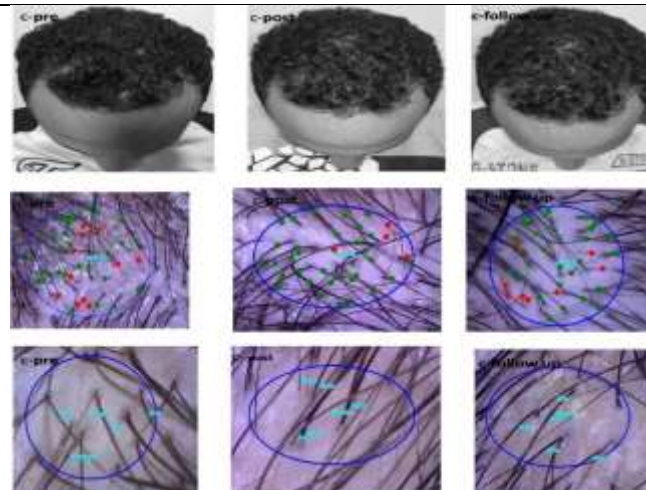
A- follow up	120.4/cm <sup>2</sup> Terminal= 31Intermediate= 6Total= 37%T= 83.8%%I= 16.2%							
Pre	1	0.072	0.073	0.074	0.085	0.06StatsAV	0.07SD	0.01
Post	1	0.112	0.123	0.094	0.075	0.06StatsAV	0.09SD	0.03
Follow up	1	0.102	0.053	0.094	0.105	0.08StatsAV	0.08SD	0.02



**Fig 3: Clinical and Follisopic Images (20x, 50x) of a patient of Group B and numbers of his Terminal & Intermediate Terminal and Vellus hairs in addition to the mean hair shaft diameter**

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Pre	87.9/cm <sup>2</sup> Terminal= 17Intermediate= 10Total= 27%T= 63.0%%I= 37.0%							
Post	113.9/cm <sup>2</sup> Terminal= 30Intermediate= 5Total= 35%T= 85.7%%I= 14.3%							
Follow up	91.1/cm <sup>2</sup> Terminal= 25Intermediate= 3Total= 28%T= 89.3%%I= 10.7%							
Pre	1	0.092	0.073	0.054	0.095	0.10StatsAV	0.08SD	0.02
Post	1	0.112	0.123	0.094	0.075	0.06StatsAV	0.09SD	0.03
Follow up	1	0.082	0.093	0.074	0.075	0.07StatsAV	0.08SD	0.01



**Fig 4: Clinical and Follisopic Images (20x, 50x) of a patient of Group C and numbers of his Terminal & Intermediate Terminal and Vellus hairs in addition to the mean hair shaft diameter**

Pre	120.4/cm <sup>2</sup> Terminal= 26Intermediate= 11Total= 37%T= 70.3%%I= 29.7%							
Post	123.7/cm <sup>2</sup> Terminal= 34Intermediate= 4Total= 38%T= 89.5%%I= 10.5%							
Follow up	120.4/cm <sup>2</sup> Terminal= 31Intermediate= 6Total= 37%T= 83.8%%I= 16.2%							

Pre	1	0.072	0.123	0.124	0.075	0.06StatsAV	0.09SD	0.03
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Post	1	0.112	0.083	0.124	0.065	0.07	StatsAV	0.09	SD	0.03
Follow up	1	0.092	0.093	0.104	0.095	0.08	StatsAV	0.09	SD	0.01

**References**

Galadari H, Shivakumar S, Lotti T, Wollina U, Goren A, Rokni GR, Grabbe S, Goldust M. Low-level laser therapy and narrative review of other treatment modalities in androgenetic alopecia. *Lasers in Medical Science*. 2020 Mar 11;11:6. PMID: 32162134 DOI: 10.1007/s10103-020-02994-4

Goren A, Sharma A, Dhurat R, Shapiro J, Sinclair R, Situm M, Kovacevic M, LukinovicSkudar V, Goldust M, Lotti T, McCoy J. Low-dose daily aspirin reduces topical minoxidil efficacy in androgenetic alopecia patients. *Dermatologic Therapy*. 2018 Nov;31(6):e12741. PMID: 30226287 DOI: 10.1111/dth.12741

Yi Y, Qiu J, Jia J, Djakaya GD, Li X, Fu J, Chen Y, Chen Q, Miao Y, Hu Z. Severity of androgenetic alopecia associated with poor sleeping habits and carnivorous eating and junk food consumption-A web-based investigation of male pattern hair loss in China. *Dermatologic therapy*. 2020 Mar;33(2):e13273. PMID: 32061036 DOI: 10.1111/dth.13273

Blumeyer A, Tosti A, Messenger A, Reygagne P, Del Marmol V, Spuls PI, Trakatelli M, Finner A, Kiesewetter F, Trüeb R, Rzany B. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*. 2011 Oct;9:S1-57. PMID: 2198098 DOI: 10.1111/j.1610-0379.2011.07802.x

Gupta AK, Foley KA. A Critical Assessment of the Evidence for Low-Level Laser Therapy in the Treatment of Hair Loss. *Dermatol Surg*. 2017 Feb;43(2):188-197. doi: 10.1097/DSS.0000000000000904. PMID: 27618394.

Badran KW, Sand JP. Platelet-rich plasma for hair loss: review of methods and results. *Facial Plast Surg Clin North Am*. 2018;26(4):469-85

Gupta M, Mysore V. Classifications of Patterned Hair Loss: A Review. *J Cutan Aesthet Surg*. 2016 Jan-Mar;9(1):3-12. doi:10.4103/0974-2077.178536. PMID: 27081243; PMID: PMC4812885.

Verma K, Tegta GR, Verma G, Gupta M, Negi A, Sharma R. A Study to Compare the Efficacy of Platelet-rich Plasma and Minoxidil Therapy for the Treatment of Androgenetic Alopecia. *Int J Trichology*. 2019 Mar-Apr;11(2):68-79. doi: 10.4103/ijt.ijt\_64\_18. PMID: 31007475; PMID: PMC6463452.

Gupta AK, Daigle D. The use of low-level light therapy in the treatment of androgenetic alopecia and female pattern hair loss. *J Dermatolog Treat*. 2014 Apr;25(2):162-3. doi: 10.3109/09546634.2013.832134. Epub 2013 Oct 9. PMID: 23924031.

Zarei M, Wikramanayake TC, Falto-Aizpurua L, Schachner LA, Jimenez JJ. Low level laser therapy and hair regrowth: an evidence-based review. *Lasers Med Sci*. 2016 Feb; 31(2):363-71. doi: 10.1007/s10103-015-1818-2. Epub 2015 Dec 21. PMID: 26690359.

Gentile P, Garcovich S. Advances in Regenerative Stem Cell Therapy in Androgenic Alopecia and Hair Loss: Wnt pathway, Growth-Factor, and Mesenchymal Stem Cell Signaling Impact Analysis on Cell Growth and Hair Follicle Development. *Cells*. 2019 May 16;8(5):466. doi: 10.3390/cells8050466. PMID: 31100937; PMID: PMC6562814.

Gentile P, Scioli MG, Bielli A, De Angelis B, De Sio C, De Fazio D, Ceccarelli G, Trivisonno A, Orlandi A, Cervelli V, Garcovich S. Platelet-Rich Plasma and Micrografts Enriched with Autologous Human Follicle Mesenchymal Stem Cells Improve Hair Re- Growth in Androgenetic Alopecia. *Biomolecular Pathway Analysis and Clinical Evaluation*. *Biomedicines*. 2019 Apr 8;7(2):27. doi: 10.3390/biomedicines7020027. PMID: 30965624; PMID: PMC6631937.

Gentile P, Garcovich S, Bielli A, Scioli MG, Orlandi A, Cervelli V. The Effect of Platelet- Rich Plasma in Hair Regrowth: A Randomized Placebo-Controlled Trial. *Stem Cells Transl Med*. 2015 Nov;4(11):1317-23. doi: 10.5966/sctm.2015-0107. Epub 2015 Sep 23. PMID: 26400925; PMID: PMC4622412.

Gentile P, Cole JP, Cole MA, Garcovich S, Bielli A, Scioli MG, Orlandi A, Insalaco C, Cervelli V. Evaluation of Not-Activated and Activated PRP in Hair Loss Treatment: Role of Growth Factor and Cytokine Concentrations Obtained by Different Collection Systems. *Int J Mol Sci*. 2017 Feb 14;18(2):408. doi: 10.3390/ijms18020408. PMID: 28216604; PMID: PMC5343942.

Gentile P, Dionisi L, Pizzicannella J, de Angelis B, de Fazio D, Garcovich S. A randomized blinded retrospective study: the combined use of micro-needling technique, low-level laser therapy and autologous non-activated platelet-rich plasma improves hair re-growth in patients with androgenic alopecia. *Expert Opin Biol Ther*. 2020 Sep;20(9):1099-1109. doi: 10.1080/14712598.2020.1797676. Epub 2020 Jul 27. PMID: 32678725.

Fertig RM, Gamret AC, Cervantes J, Tosti A. Microneedling for the treatment of hair loss? *J Eur Acad Dermatol Venereol*. 2018 Apr;32(4):564-569. doi: 10.1111/jdv.14722. Epub 2017 Dec 21. PMID: 29194786.

Esmat SM, Hegazy RA, Gawdat HI, Abdel Hay RM, Allam RS, El Naggar R, Moneib H. Low level light-minoxidil 5% combination versus either therapeutic modality alone in management of female patterned hair loss: A randomized controlled study. *Lasers Surg Med*. 2017 Nov;49(9):835-843. doi: 10.1002/lsm.22684. Epub 2017 May 10. PMID: 28489273.

Rossi A, Cantisani C, Melis L, Iorio A, Scali E, Calvieri S. Minoxidil use in dermatology, side effects and recent patents. *Recent Pat Inflamm Allergy Drug Discov*. 2012 May;6(2):130-6. doi: 10.2174/187221312800166859.



PMID: 22409453.

Davies GC, Thornton MJ, Jenner TJ, Chen YJ, Hansen JB, Carr RD, Randall VA. Novel and established potassium channel openers stimulate hair growth in vitro: implications for their modes of action in hair follicles. *Journal of investigative dermatology*. 2005 Apr 1;124(4):686-94. ISSN: 0022-202X

Badran FK, Abd El Maksoud RE, Moawad MM. The efficacy of topical minoxidil 2% versus topical botanically derived inhibitors of 5 alpha reductase in treatment of female pattern hair loss by trichoscopy. *Journal of the Egyptian Women's Dermatologic Society*. 2019 Sep 1;16(3):184. DOI: 10.4103/JEWD.JEWD\_31\_19

Varothai S, Bergfeld WF. Androgenetic alopecia: an evidence-based treatment update. *Am J Clin Dermatol*. 2014 Jul;15(3):217-30. doi: 10.1007/s40257-014-0077-5. PMID: 24848508.

Jimenez JJ, Wikramanayake TC, Bergfeld W, Hordinsky M, Hickman JG, Hamblin MR, Schachner LA. Efficacy and safety of a low-level laser device in the treatment of male and female pattern hair loss: a multicenter, randomized, sham device-controlled, double-blind study. *Am J Clin Dermatol*. 2014 Apr;15(2):115-27. doi: 10.1007/s40257-013-0060-6. PMID: 24474647; PMCID: PMC3986893.

Avram MR, Rogers NE. The use of low-level light for hair growth: part I. *J Cosmet Laser Ther*. 2009 Jun;11(2):110-7. doi: 10.1080/14764170902842531. PMID: 19466643.

Lohr NL, Keszler A, Pratt P, Bienengraber M, Warltier DC, Hogg N. Enhancement of nitric oxide release from nitrosyl hemoglobin and nitrosyl myoglobin by red/near infrared radiation: potential role in cardioprotection. *J Mol Cell Cardiol*. 2009 Aug;47(2):256-63. doi:10.1016/j.yjmcc.2009.03.009. Epub 2009 Mar 25. PMID: 19328206; PMCID: PMC4329292.

Cervantes J, Perper M, Wong LL, Eber AE, Fricke AC, Wikramanayake TC, Jimenez JJ. Effectiveness of platelet-rich plasma for androgenetic alopecia: A review of the literature. *Skin appendage disorders*. 2018;4(1):1-1. <https://doi.org/10.1159/000477671>

