Journal of Pakistan Association of Dermatologists. 2020; **30(3)**: 375-381.

Original Article

Efficacy and safety of platelet rich plasma therapy in male androgenetic alopecia

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Abstract

Background Androgenetic alopecia (AGA) is a common hair loss disorder affecting both men and women. Despite multiple therapeutic options, treatment of AGA remains unsatisfactory. Platelet-rich plasma (PRP) is an autologous concentrate of plasma with a greater count of platelets than that of whole blood and is effective in promoting hair regrowth.

Objective This randomized controlled clinical trial was conducted to evaluate the efficacy and safety of PRP therapy in male androgenetic alopecia (AGA).

Materials and Methods This study was conducted at the Department of Dermatology & Venereology, Bangabandhu Sheikh Mujib Medical University from October, 2016 to October, 2017. Fifty four male patients with AGA diagnosed by dermatologist were enrolled by consecutive sampling. The participants were divided into two groups by odd (group- A) and even numbering (Group-B). Group-A patients were treated with PRP injections on their scalp at 4 weeks interval for 3 sessions and group-B patients were treated with topical 5% minoxidil lotion for the same duration. All patients were followed up at 8th and 12th week. At each follow-up hair was counted in prefixed area of treatment, history was taken and clinical examinations were performed to detect any adverse effects of these therapies.

Results Among 54 male AGA patients, there was no significant difference (P>0.05) in mean age. Positive family history of AGA was found in 74.04% and 70.37% patients in group-A and group-B respectively. According to Norwood- Hamilton classification, in group-A 29.63% patients were in Stage II and in group-B 25.93% patients were in stage II. At the beginning, in group-A and group-B mean hair count/sq.cm was 15.41±1.16 and 15.56±1.88 respectively. At 8th week, mean hair count/sq.cm of group-A and group-B was 17.42±1.10 and 16.15±1.87 and at 12th week, the hair growth of group-A was increased to 19.14±1.06/sq.cm which was significantly higher (P<0.05) compared to group-B (17.62±2.07/sq.cm). 81.48% patient complaints mild pain followed by erythema at the injection site in group-A and 66.66% patient complaints of transient hair fall at the beginning in group-B.

Conclusion PRP was more efficacious than topical 5% minoxidil lotion in male AGA.

Key words
Platelet Rich Plasma (PRP), androgenetic alopecia (AGA), efficacy.

Introduction

Androgenetic alopecia (AGA) is a common chronic hair loss disorder which is characterized by progressive hair loss, affecting both sexes. It affects up to 80% Caucasian men and 40% women.[1] It may start at puberty and progress with age.[2] There is a significant impairment of quality of life in Patients with AGA, as hair is considered to be an important feature of self-

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image independent of age and gender. Hair loss affects personal attractiveness and self–image. It may cause depression and other negative effects on life. There are number of products prescribed by the dermatologists for the treatment of AGA.[3] Minoxidil and Finasteride are Food and Drug Administration (FDA) approved drugs for AGA. Minoxidil prolongs anagen and increases hair follicle size through stimulation of potassium channels and prostaglandin endoperoxide synthase-1, which increases level of prostaglandin E2 (PGE2).[4] Minoxidil promotes the survival of dermal papilla cells by increasing Bcl-2/Bax ratio and by activating ERK and Akt.[5] Oral finasteride induces the prolongation of anagen phase of hairs, which results in gradual thickening and elongation of the hairs.[6] Finasteride reduces the pattern hair loss associated with increased expression of caspases[7] and apoptosis inhibitors and for this reason it is suggested to activate anagen hair growth.[8] Both of these two drugs can be used alone or in combination. Continued uses of these two drugs beyond 2 years do not promote continued hair regrowth. Despite of the availability of drug therapies, patient compliance is low and satisfaction rate regarding the outcome of drug therapies is poor. There is also a lot of topical and important systematic adverse effects lead to the search of new treatment options for AGA. PRP is an autologous preparation of platelets concentrated in plasma (3-7 times enrichment) with a platelet concentration more than 1,000,000 platelets/L.[2] PRP has been attracted attention in several medical fields as well as in dermatology for its skin rejuvenating effects, rapid healing, reduced infection, decreased chance of hypertrophic keloids and scars. Activation of alpha granules of platelets through coagulation releases numerous proteins, including platelet-derived growth factor (PDGF), transforming growth factor (TGF-β), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), epidermal growth factor (EGF) and interleukin (IL)-1 which produce mitogenic effects in various cells.[1] Growth factors (GFs) released from platelets may act on stem cells in the bulge area of the follicles, stimulating the development of new follicles and promoting neovascularization.[9] The regenerative potential of PRP depends on the levels of growth factors released. Main GFs involved in androgenetic alopecia are platelet-derived growth factor (PDGF), transforming growth factor (TGF-β), vascular endothelial growth factor (VEGF) and insulin-like growth factor (IGF) with their isoforms. GFs bind to their respective receptors located in stem cells in the bulge area of the follicle. In the bulge area, primitive stem cells of ectodermal origin are found, giving origin to epidermal cells and sebaceous glands. In matrix, germinative cells of mesenchymal origin are found at the dermal papilla (DP). Interactions between these two cells and binding of growth factors (PDGF, TGF-β and VEGF) activate the proliferative phase of the hair giving rise to new follicular unit.[9] Therefore PRP could be a potential treatment of AGA. This study was carried out to evaluate the efficacy and safety of PRP therapy.

Materials & Methods

This randomized controlled clinical trial was conducted at the Department of Dermatology & Venereology, Bangabandhu Sheikh Mujib Medical University from October, 2016 to October, 2017. The protocol got approval of the 'Institutional review board' of the university vide memo no BSMMU/2017/554 dated 16/01/2017. Informed consent was taken from each of the study subjects before enrolling them in the study. Patients were diagnosed clinically by the dermatologist. Fifty four males with AGA aged from 18 to 50 years were included. The patients with a history suggestive of immunosuppression (malignancy,

chemotherapy, steroid therapy etc.), known dermatological diseases affecting the scalp, autoimmune disorders, hematologic disorders, platelet dysfunction syndrome, hypertension, DM and patients on anticoagulation therapy were excluded. History regarding age, age of disease onset, family history, duration of the disease, history of any other dermatological or systemic diseases which might cause hair fall and clinical examination like hair pull test was done for each and every patient. The study population was enrolled by consecutive sampling and divided in two groups by odd (Group-A) and even (Group-B) serial number of patients. Baseline hair count of affected area (5 sq.cm of right vertex), complete blood count, random blood sugar, bleeding time and clotting time of all patients were done at first visit. Using Norwood–Hamilton classification, patients were categorized into stage I to stage VII. All informations were noted in a predesigned data collection sheet. Patients of group-A was treated with PRP therapy and group-B was treated with topical 5% minoxidil lotion. To prepare 1 ml PRP, under aseptic precaution 18 cc of whole blood was collected from patient's peripheral vein and was mixed with 2 cc sodium citrate in a vaccutainer tube. The tube was rotated in a centrifugation machine at 1100 revolutions per minute for 10 minutes. This centrifugation allowed blood separation into three layers, namely bottom RBC layer (55% of total volume), topmost acellular plasma layer called platelet poor plasma (PPP, 40% of total volume) and an intermediate PRP layer (5% of total volume). Then PRP was collected in a syringe from intermediate layer.[10] Required amount of PRP was prepared according to affected site of the patient. One hour prior to administration of PRP, local anesthetic agent (Xyloken 10% spray) was applied over the bald area. Area of the scalp to be treated was cleaned with hexisol (Chlorhexidine gluconate in isopropyl alcohol 0.5%+70% solution) followed by povidone-iodine. With the help of 100 unit insulin syringe PRP was injected 0.1ml/sq.cm of affected area by Nappage technique (Series of injections 1 centimeter apart, 2-3 millimeter depth with syringe at $30\text{-}60^0$angle) in a minor operating theatre at the Department of Dermatology & Venereology, BSMMU under aseptic precaution at 4 weeks interval for 3 sessions (0 week, 4^{th} week, 8^{th} week). Patients were advised not to take any other medication since it might affect the effect of PRP. Group-B was treated with 5% topical minoxidil solution (Xenogrow 5% solution, Incepta pharmaceuticals limited, Bangladesh) sprayed over the affected area of scalp 1 ml (7 spray) twice in a day (Twelve hourly) for same duration.

Hair count over the prefixed area (5 sq.cm of right side of vertex) and adverse reactions were noted at 8^{th} and 12^{th} week. Subjective improvements of patients were documented on a scale of worst (0) to best (3).

Quantitative data were presented as mean values±SD, and qualitative data as percentage (%). Means were compared by the Student t test, and percentages were compared by Z-test of proportion. All statistical analyses were performed using the SPSS software 22. $p \leq 0.05$ was considered significant.

Results

Fifty four patients were grouped into two groups (Group-A and group-B). Majority in group-A (48.2%) was in the age group of 18-30 years. The mean age of the patients is 31±7.88 years in group-A and 35.44±8.88 years in group-B and there is no significant difference (P>0.05) in these two groups **(Table 1)**. Positive family history of AGA in group-A and in group-B were 74.04% and 70.37% respectively **(Table 2)**. According to Norwood-Hamilton classification, in group-A, the most frequent pattern is found in

Table 1 Distribution of the study patients by age (n=54)

Age	*Group-A (n=27)*	*Group-B (n=27)*	*p-value*
18-30 yr	13(48.2%)	7(25.92%)	0.061^{ns}
31- 40 yr	12(44.44%)	12(44.44%)	
41- 50 yr	2(7.2%)	8(29.62%)	
Mean ± SD	31±7.88	35.44±8.88	

Data are expressed as frequency, percentage, mean±SD

Table 2 Distribution of the study patients by family history of AGA (n=54)

Family history of AGA	*Group-A (n=27)*	*Group-B (n=27)*
Positive	20 (74.04%)	19 (70.37)
Negative	7 (25.92%)	8 (29.62

Table 3 Clinical evaluation of study patients according to Norwood–Hamilton classification (n=54)

Stages of AGA	*Group-A (n=27)*	*Group-B (n=27)*	*p-value*
Stage-I	3 (11.11%)	4 (14.82%)	1.0^{ns}
Stage-II	8 (29.63%)	7 (25.93%)	
Stage-III	7 (25.93%)	4 (14.82%)	
Stage-IV	3 (11.11%)	2 (7.40)	
Stage-V	4 (14.82%)	6 (22.22%)	
Stage-VI	2 (7.40%)	3 (11.11%)	
Stage-VII	-	1 (3.70%)	

Table 4 Patient's subjective evaluation of hair growth at 12 weeks (n=54)

Patient's self-assessment scale	*Group-A (n=27)*	*Group-B (n=27)*
0=no change	1 (3.70%)	3 (11.12%)
+1=Mild improvement	4 (14.81%)	8 (29.63%)
+2=Moderate improvement	14 (51.85%)	9 (33.33%)
+3=marked improvement	8 (29.64)	7 (25.92%)

Table 5 Evaluation of hair growth by hair count/sq.cm (Mean ± SD)

Stages of evaluation	*Group-A (n=27) (Mean±SD)*	*Group-B (n=27) (Mean±SD)*	*P value*
Baseline	15.41±1.16	15.56±1.88	0.742 (P>0.05)
At 8th week	17.42±1.10	16.15±1.87	0.004^{s} (P<0.05)
At 12th week	19.14±1.06	17.62±2.07	0.002^{s} (P<0.05)

Table 6 Side effects of study patients (n=54)

Side effects	*Group-A (n=27)*	*Group-B (n=27)*
Transient increase in hair fall	Nil	18 (66.66)
Headache	1 (3.70%)	6 (22.22)
Sticky scalp	Nil	4 (14.81)
Mild pain and erythema	22 (81.48%)	Nil

Stage II (29.63%) and in group-B, 25.93% patients are in stage II. There is no significant difference (p =1.0) in stages of AGA in between these two groups **(Table 3)**. According to the patients' own evaluation majority achieved a moderate improvement. Group-A and group-B patients had moderate improvement in 51.85%. and in 33.33% respectively **(Table 4)**. Baseline mean hair count per sq.cm for group-A and group-B was 15.41±1.16 and 15.56±1.88 respectively with no significant difference (P>0.05). After treatment, at 8th week the mean hair count of group-A and group-B were increased to 17.42±1.10 and 16.15±1.87 respectively. Hair growth of group-A was significantly higher (P<0.05) than that of group-B at 8th week. After treatment at 12th week, the hair growth of group-A was increased to 19.14±1.06 which was significantly higher (P<0.05) in comparison to group-B (17.62±2.07) **(Table 5)**. 81.48% of group-A patients had mild pain and erythema during PRP injection andn66.66% of group-B patients experienced transient hair loss at early stages **(Table 6)**.

Graphical representation of hair growth up to 12 weeks showed similar baseline hair count per sq.cm but at 8thand 12th weeks. Group-A demonstrated more hair growth (17.42±1.10) and (19.14±1.06) than that of group-B (16.15±1.87) and (17.62±2.07) respectively. Here the graph showed upward drift for PRP therapy in compared with topical 5% minoxidil solution **(Figure 1)**.

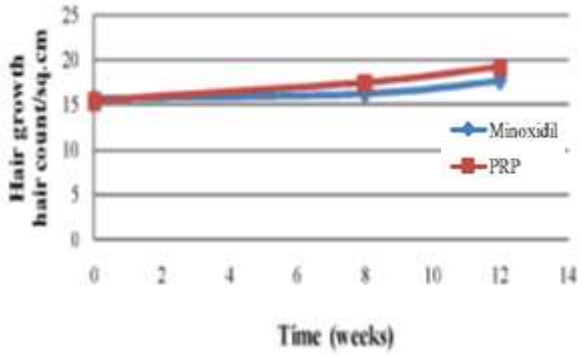

Figure 1 Graphical representation of hair growth up to 12 weeks

Discussion

In our study majority of the patients (48.2%) were of 18-30 years age in group-A. Most of the patients in group-A (51.85%) showed moderate improvement **(Table 1 & 4)**. In a study, Patel *et al*.[11] treated 220 males (110 patients with PRP and another 110 patients with topical 2-5% minoxidil lotion) and hair growth was measured after 3 months of first treatment. They reported 74% patients in PRP group and 70% patients in minoxidil group were from 20-30 years of age range and showed good response in 91.20% in PRP group that was statistically significant (p=0.000647). Though majority of our group-A patients showed moderate improvement but the percentage of improvement is much less than that of Patel *et al*.[11] They activated the PRP by adding calcium gluconate (1 part calcium gluconate plus 9 part PRP) before injections. Use of activated PRP might be the cause of good response in increased number of patients. After treatment, hair count/sq.cm in group-A was significantly higher ($p<0.05$) than that of in group-B at 8th week (17.42±1.10 vs 16.15±1.87). At 12th week after the treatment, the hair count/sq.cm of group-A also was significantly higher ($P<0.05$) in comparison to group-B (19.14±1.06vs17.62±2.07) **(Table 5)**. There was a significant increase rate in hair density of 19.29% and 9.19% at 3 and 6 months respectively. All of the patients did not show improvement, varied from no improvement to significant improvement. Hair density followed an upward curve, reached a peak at 3 months, decreased at 6 months but value at each level was significantly higher than that of baseline.[12] Our study revealed that AGA patients with grade II-III (according to the Hamilton-Norwood scale) had better response compared to patients with advanced alopecia with both PRP and minoxidil lotion. Gkini MA *et al*.[12] also reported similar observations and commented this regarding their study outcome. In accordance with our study, Gkini MA *et al*.[12] reported that patients declared an overall positive satisfaction. In this study, PRP treated patients showed significant improvement compared to topical 5% minoxidil lotion treated patients. Taieb *et al*.[13] found that PRP was more effective in the treatment of alopecia than topical minoxidil 5% which was similar to our finding. According to the experiment of James *et al*.[14] three months after the treatment with PRP, the patients presented clinical improvement in the hair counts, hair thickness, hair root strength and overall alopecia that was concordant to our study outcome. In a study Garg S *et al*.[15] reported that in PRP group, all [twenty] subjects had more than 75% hair re-growth at 6 months. This also supports our results. Singhal P *et al*.[16] reported that three months after the autologous PRP treatment, the patients presented clinical improvement in the hair counts, hair thickness, hair root strength, and overall alopecia. Our study result also show similar outcome. Kang JS *et al*.[17] concluded that PRP preparations have a positive effect on male and female pattern hair loss. The conclusion is related with the result of our study though there was no female patient in this study.

In our study mild pain followed by erythema at injection site was reported in 81.48% of patients and head ache in 3.7% in group-A. In group-B transient hair fall, head ache and stickiness of scalp were complained by 66.66%, 22.22% and

14.81% respectively. None discontinued the treatment due to adverse events. Similar findings were observed by Gkini MA *et al.*[12] in PRP group. Their reports revealed that during the PRP injections, 100% of the patients felt mild pain, though they were anesthetized with local anesthetics. Only one-fourth of them had pain after the procedure that subsided after 4 hours. None reported any worsened hair shedding, infection or ecchymosis.[12]

Conclusion

PRP therapy is more effective in the treatment of androgenetic alopecia in male, without remarkable adverse effects, while this therapy accompanied by a high patients' satisfaction rate than that of topical 5% minoxidil lotion. PRP injection for androgenic alopecia is a simple, cost-effective treatment option for hair loss and can be regarded as a valuable treatment modality for androgenic alopecia.

Limitations of the study

Sample size was small. It was conducted in a single tertiary care hospital which may not represent the general population. Long term follow-up was not done.

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