Original Article

Effect of Platelet-Rich Plasma on Clinical Outcomes of Androgenic Alopecia

Haque MA[1], Shawkat SM[2], Aslam AB[3], Abdullah MS[4]

Conflict of Interest: None
Received: 14.03.2021
Accepted: 04.11.2021
www.banglajol.info/index.php/JSSMC

Abstract:

Background: *Androgenetic alopecia (AGA) also known as male pattern baldness is the most common hair loss disorder characterized by chronic, nonscarring disorder that is marked by a progressive reduction in the diameter, length, and pigmentation of the hair. This disorder is located primarily on the central scalp with various patterns of loss. Pathophysiological features include an alteration in the hair cycle via reduction of the anagen (growth) phase, inflammation, and follicular miniaturization. Therapies for AGA are limited and there is no cure. There is a high demand for hair restoration. Platelet-rich plasma (PRP), a treatment modality shown to promote wound healing, has also been explored as a treatment for AGA.*

Objectives*: To observe the effectiveness of platelet-rich plasma for Androgenetic Alopecia.*

Materials & method: *This prospective observational study was conducted among 30 subjects with androgenetic alopecia from July 2018 to June 2020 in a reputed private hospital in Dhaka. Five platelet-rich plasma (PRP) treatments, at intervals of 4 –5 weeks, and 2 follow-up examinations were performed. Blood (9 cc) from each AGA patient was collected in 10 cc syringe, and PRP was isolated using commercially available kit under sterilized conditions. Isolated PRP was injected in the bald areas of scalp of AGA patients. Treatment efficacy was assessed by changes in hair number and diameter. A secondary objective was to assess clinical improvement, which was evaluated by 5-point Likert scale. Then variables were analyzed and compared. Data was processed and analysed with the help of computer program SPSS and Microsoft excel. Quantitative data expressed as mean and standard deviation and qualitative data as frequency and percentage. Comparison was done by tabulation and graphical presentation in the form of tables, pie chart, graphs, bar diagrams, histogram & charts etc.*

Result*: It was found that majority of the patients i.e. 41(68.3%) were in the age group 20-40 years, mean age was found to 38.3±6.5 years. No significant difference in age and other demographic profile was observed between groups. The median (range) hair number per square centimetre at baseline was 38.0 (13-105) in the both groups. At the final follow-up visit, hair number is improved & it was found 53.0 (24-130) in the treated group and 41.0 (11-105) in the control group. Differences was statistically significant (p=0.017). Hair diameter (μm) at baseline was 65.0 (48-81) μm in the treated group and 66.0 (49-75) in the control group. At the final follow up visit, hair diameter also improved and it was 80.0 (58-94) μm in the treated group and 69.0 (51-85) μm in the control group. Differences was statistically significant (p=0.031). There were no treatment-related adverse effects.*

Conclusion*: Present study concluded that PRP is an effective treatment option in androgenetic alopecia, provides better clinical outcome in terms of improve hair density, diameter and significant subject satisfaction.*

Key Words:
Androgenic alopecia, Platelet-rich plasma (PRP).

[J Shaheed Suhrawardy Med Coll 2021; 13(2): 158-163]
DOI: https://doi.org/10.3329/jssmc.v13i2.65179

1. Dr. Mohammad Anwarul Haque, Medical Officer, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka
2. Dr. Sabbir Muhammad Shawkat, Consultant, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka
3. Dr. Azmiree Binte Aslam, Assistant professor (CC), Shahabuddin Medical College, Dhaka, Bangladesh
4. Dr. Mohammad Shayekh Abdullah, Resident Physician, Department of Medicine, Dhaka Medical College Hospital, Dhaka

Correspondence to: Dr. Mohammad Anwarul Haque, Medical Officer, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh, Phone: +8801711615174, E-mail: dr_sumon2005@yahoo.com

Introduction:

Androgenetic alopecia (AGA) is a hair loss disorder affecting 80% of men and 50% of women throughout their lifetime[1]. AGA is determined by genetics and influenced by hormones. The key hormone is dihydrotestosterone (DHT), a metabolite of testosterone, which activates androgen receptors. In men, testosterone is converted to DHT by 5á-reductase, while dehydroepiandrosterone and other weaker androgens are the precursors of DHT in women. Hair follicles in the scalp vertex and frontotemporal areas have an increased density of androgen receptors; hence, they exhibit a greater response to DHT and experience increased hair loss in AGA[2].

Currently, the Hamilton-Norwood classification is the standard system for classifying different stages of AGA[3]. Hamilton first proposed a detailed system grading severity of hair loss based on frontoparietal and frontal recessions as well as frontal thinning in 1951. The grading system was based on 8 evolutionary types of hair loss and 3 subgroups: types I-III described scalps which were not bald, while types IV-VII classified bald scalps. Later, in 1975, Norwood expanded on Hamilton's system by creating the Hamilton-Norwood classification, which encompassed major patterns of hair loss, but also rarer patterns of male pattern balding. The Hamilton-Norwood system includes 7 types of hair loss, as well as information about a type A variant, based on the notion that thinning begins in the temples and crown/vertex and continues to encompass the entire top of the scalp[4]. The Ludwig classification system is used to describe the severity of AGA in women. Ludwig based the system on 3 grades of hair loss and emphasized the preservation of the frontal fringe despite progressive centrifugal loss over the upper portion of the scalp in females[4, 5]. Nevertheless, he did not account for the accentuation of frontovertical alopecia in his classification - this information was later described by Olsen in her own classification[4, 6].

The current standard of treatment for AGA includes oral finasteride and topical minoxidil solution or foam in males and minoxidil solution or foam in females[7]. Additional therapies including dutasteride, ketoconazole, prostaglandin analogues, and hormonal therapy have also been used in treating AGA. Unfortunately, current therapies are not effective for all subjects with AGA. On the one hand, medication is required for an indefinite period of time, and effectiveness is limited by patient adherence. In addition, they may cause side effects such as hypertrichosis close to the area of minoxidil application, and possible birth defects, decreased libido, and prolonged impotence with finasteride use in males[8]. On the other hand, because of its invasive nature and high price, surgeries such as hair transplantation and scalp reduction are generally reserved for patients who do not achieve success with medical therapy. Recently, Platelet-rich plasma (PRP) treatment has gained popularity in treatment of androgenetic alopecia (AGA).

Platelet-rich plasma (PRP), a new biotechnology, is the product of a heightened interest in cell-based therapy and tissue engineering. This therapy is defined as an autologous preparation of plasma with concentrated platelets. PRP contains various growth factors and cytokines that enhance the body's inherent capacity to repair and regenerate[9, 10]. Research has demonstrated the beneficial effects of PRP, such as proliferation of adipose precursor cells, wound repair, cellular differentiation, and angiogenesis[9]. The principle behind PRP treatment is to enrich the platelets through centrifugation, to reverse the RBC-to-platelet ratio to achieve a 94% concentration of platelets and a 5% concentration of RBCs. The high level of growth factors and cytokines in PRP are thought to facilitate tissue rejuvenation and healing[10]. Recent study demonstrated that PRP is effective for treatment of Androgenetic alopecia[11]. Meta-analysis shows a significantly locally increased hair number per cm^2 was observed after PRP injections versus control. Similarly, a significantly increased hair thickness cross-section per 10"4 mm^2 favoring PRP group[12].

Platelets are most often thought of for their hemostatic functions. However, they also contain a vast reservoir of over 800 proteins which, when secreted, act upon numerous targets including stem cells, fibroblasts, osteoblasts, endothelial, and epithelial cells. Granulation of these factors generally begins within 10 min of platelet activation. Besides platelets and their secreted factors, there are other active components within PRP, importantly fibrinogen and leukocytes. The current thinking is that the therapeutic benefits of PRP come not only from the platelets, but from the combination of constituents and growth factors[13].

PRP contains high concentrations of over 20 growth factors that are actively secreted from the á-granules of platelets. Among those thought to stimulate hair regrowth are platelet-derived growth factor, transforming growth factor, vascular endothelial growth factor (VEGF), epidermal growth factor, fibroblast growth factor, connective tissue growth factor, and insulin-like growth factor IGF-1[14]. These essential proteins regulate cell migration, attachment, proliferation, and differentiation and promote extracellular matrix accumulation. Growth factors in PRP promote hair regrowth by binding to their respective receptors expressed by stem cells of the hair follicle bulge region and associated tissues. Upon ligand binding, stem cells induce the proliferative phase of the hair follicle, producing the anagen follicular unit and facilitating hair

regrowth. Further, they activate downstream cascades leading to angiogenesis and stimulation and generation of adnexal structures. Anagen-associated angiogenesis has been linked to the secretion of VEGF by keratinocytes in the outer root sheath and fibroblasts of the dermal papilla. This increased production of VEGF promotes the growth of normal and pathological dermal structures[15]. Activated autologous PRP has also been noted to activate the proliferation of dermal papilla cells by upregulating fibroblast growth factor-7 and â-catenin, in addition to extracellular signal-related kinase and Akt signaling[15]. PRP showed excellent efficiency as a novel therapy of androgenic alopecia through hair density evaluation[16].

Methodology:

This prospective observational study was conducted among patients with androgenetic alopecia. Informed written consent was obtained from each participant. Selection criteria was subjects with untreated AGA, aged 18–52 years and selected subjects had an AGA Norwood-Hamilton score of e"III. Exclusion criteria includes previous or ongoing treatment for AGA (finasteride, minoxidil), previous hair transplantation, malignancy, haematological disorders, thyroid dysfunction, malnutrition, and other dermatological disorders contributing to hair loss. Five treatments were performed at intervals of 4–5 weeks. Thirty subjects were treated with PRP (Group A or treatment group) and 30 with conventional treatment (Group B or control group), by Tab. Finasteride & Minoxidil spray. Hair density and hair number were evaluated at 3 time-points: baseline (or pretreatment) and at follow-up visits 3 months after treatment and 6 months after the last treatment.

Study procedure: At each treatment, 20 ml of each subject's blood was collected in a tube containing sodium citrate to stop clotting. Platelet-poor plasma (PPP) and red blood cells were removed from the blood using "Yes" PRP kits, centrifuging at 2,800 RPM for 9 min (single-spin procedure) and the resulting PRP was extracted into a syringe. During the same session, depending on the degree of AGA, approximately 3–4 ml of the concentrated PRP, was used to intracutaneously deliver 0.1 ml injections into the affected areas of the scalp. The injections were delivered with a 30-gauge needle at approximately 1 cm intervals in a grid-like pattern.

Outcome measures: The main outcome measures were hair number per square centimetre and hair diameter (μm), both measured by visual and photographic assessment. Briefly, images of a shaved area of the scalp (1 cm^2) were taken with a digital camera and evaluated for determination of the essential parameters of hair growth. The secondary objective was the clinical improvement, which was evaluated subject satisfaction by 5-point Likert-type scale. Statistical analysis of the data was done using statistical processing software (SPSS). A p-value <0.05 was considered result significant.

Result & Observation:

Total of 60 patients fulfilling inclusion/exclusion criteria were studied. Results and observations are given below.

Table I

Demographic data of the patients (n=60)

Demographic data	Group A (n=30)	Group B (n=30)	Total & Percentage
Age (years)			
20-40	21(70.0%)	20(66.7%)	41(68.3%)
41-60	9(30.0%)	10(33.3%)	19(31.7%)
Mean ± S.D.			38.3±6.5
Occupation			
Service holder	9(30.0%)	12(40.0%)	21(35.0%)
Business	16(53.3%)	15(30.0%)	31(51.7%)
Student	3(10.0%)	2(6.7%)	5(8.3%)
Others	2(6.7%)	1(3.3%)	3(5.0%)

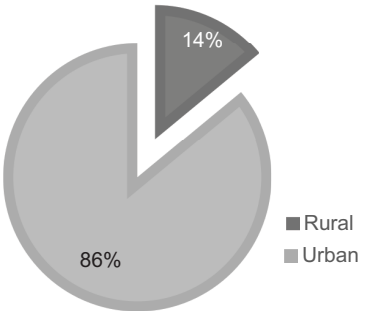

Figure 1: *Distribution of patients according to residence*

Table I shows the demographic data of the patients. Majority of the patients i.e. 41(68.3%) were in the age group 20-40 years, mean age was found to 38.3±6.5 years. Maximum patients (e.g., 51.7%) were businessman, service holder 35.0%. No significant differences (p=0.981) were found between groups with respect to demographic characteristics.

Figure 1 shows the residency of study subjects. Maximum patients (86%) came from urban areas.

Table II

Evaluation of clinical efficacy by objective assessment (n=60)

Variables	Group A (n=30) Median (range)	Group B (n=30) Median (range)	P value
Hair number (per cm^2)			
Baseline	38.0 (13-105)	38.0 (15-102)	1.000
At 1st follow up	47.5 (18-125)	36.0 (8-95)	0.065
At final follow up	54.0 (24-130)	41.0 (11-105)	0.017

Table-III

Evaluation of clinical efficacy by subjective assessment (n=60)

Impression	Satisfaction grade (Likert Scale)	Group A (n=30)	Group B (n=30)	P value
Very satisfied	5	8 (26.7)	3 (10.0)	
Somewhat satisfied	4	19 (63.3)	12 (40.0)	
Undecided/ neutral	3	3 (10.0)	9 (30.0)	
Somewhat dissatisfied	2	0	6 (20.0)	
Very dissatisfied	1	0	0	
mean±SD		4.16±0.7	3.43±0.7	0.001

Table II shows evaluation of clinical efficacy by objective assessment. The median (range) hair number per square centimetre at baseline was 38.0 (13-105) in the both groups. At the first follow-up visit, hair number was 47.5 (18-125) in the treated group and 36.0 (8-95) in the control group. Differences to baseline were 6.5 in the treated group and –2.0 in the control group. At the final follow-up visit 6 months after the last treatment, hair number was 53.0 (24-130) in the treated group and 41.0 (11-105) in the control group. Differences to baseline were 16.0 in the treated group and 3.0 in the control group; these differences were statistically significant (p=0.017)

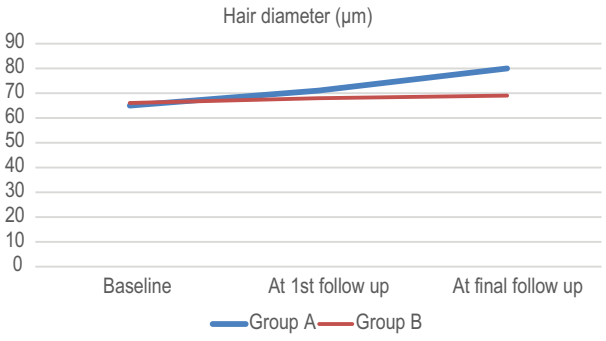

Figure 2: *Assessment of Hair diameter (µm) after treatment (n=60)*

Figure 2 shows the comparison of Hair diameter (µm) after treatment. The median (range) hair diameter at baseline was 65.0 (48-81) micrometres in the treated group and 66.0 (49-75) in the control group. At the first follow-up visit, hair diameter was 71.0 (51-83) micrometres in the treated group and 68.0 (51-83) micrometres in the control group. Differences to baseline were 3.0 micrometres in the treated group and 2 micrometres in the control group. At the final follow up visit 6 months after treatment, hair diameter was 80.0 (58-94) micrometres in the treated group and 69.0 (51-85) micrometres in the control group. Differences to baseline were 15 micrometres in the treated group and 3 micrometres in the control group; these differences were also statistically significant (p=0.031).

In this study 5(five) point Likert Scale was used to assess the patient's satisfaction. The Likert Scale is a rating scale that's often used assessing the patients/ subject regarding experiences and overall effectiveness with the sort or service. Total 27(90.0%) patients in group A experienced/ satisfaction of grades 4 and 5 after treatment, whereas 15(50.0%) patients in group B experienced/ satisfaction of grades 4 and 5 after treatment. The mean±SD of score was 4.16±0.7 in group-A and 3.43±0.7 in group-B. So, treatment of androgenic alopecia with platelet-Rich Plasma is associated with better outcome. The difference was statistically significant ($p<0.05$) between groups.

Table IV

Evaluation of any complication (n=60)

Complications	Group A (n=30)	Group B (n=30)	Total
Itching	0	0	0
Pain	2	0	2
Swelling/ oedema	2	0	2
Erythema	0	0	0
Folliculitis	0	0	0
Scaling	0	0	0
Fever	0	0	0
Urticaria	0	0	0

There were no treatment-related adverse effects such as itching, erythema, folliculitis, or scaling. Some participants reported mild headache, tolerable and temporary pain during treatment and transient edema after PRP treatment.

Discussion:

In recent years, PRP has become an increasingly popular treatment modality for various dermatological and aesthetic indications, including hair restoration. Present study reported the promotion of hair growth by PRP, indicating that PRP may offer hope to those affected by hair loss. Our findings were consistent with result of other studies. Some of these findings are discussed in more detail below.

A recent pilot study by Anitua et al[17] evaluated the use of plasma rich in growth factors in 19 subjects with AGA. Subjects were given 5 injections of PRP enhanced with platelet-rich growth factor (PRGF) activator to provoke release of growth factors and morphogens from the specimen. Compared to baseline, all outcome measures showed positive results after 1 year of follow-up. Mean hair density, hair diameter, and terminal/vellus hair ratio were among the measures showing statistically significant improvement ($p < 0.05$). Histomorphometric evaluation also favored the use of PRP, showing improvement in epidermal thickness, perifollicular neoangiogenesis, and terminal/miniaturized hair ratio, as well as decreased perivascular inflammatory infiltrates. Overall, patients were satisfied with their clinical improvement.

Alves and Grimalt[18] led a 25-subject randomized, blinded, half-head investigation, among which 22 completed the trial. The subjects were divided into 2 groups: group A, which received 3 mL of PRP on the right half of the head and 3 mL of saline placebo on the left, and group B, which received the same 2 solutions on opposite sides of the head. After 3 and 6 months, statistically significant improvements were detected in mean anagen hairs, mean telogen hairs, hair density, and terminal hair density in PRP-treated areas when compared with baseline ($p < 0.05$). Mean total hair density was the only measure found to be significantly increased in PRP versus placebo-treated areas ($p < 0.05$).

Another randomized, blinded, half-head study performed by Gentile et al[19] evaluated treatment outcomes of PRP in 20 male subjects. PRP was injected on half of the affected scalp of each patient, while the other side received physiological solution as control. The study found a statistically significant increase in all outcome measures, including mean hair count, hair density and terminal hair density, after 3 months of PRP treatment compared to placebo. Cervelli et al.[17] performed a very similar study to that of Gentile's group with 10 men, and found similar positive results after 3 months of PRP. All outcome measures showed statistically significant improvement.

Singhal et al[8] conducted a small controlled clinical trial to compare PRP with medical treatment in 20 subjects, 8 males and 2 females in each treatment group. Hair growth was seen in 6 subjects after just 7 days, but in 4 subjects after 15 days. Yet, by the end of 3 months, all evaluated parameters showed superior outcomes in PRP-treated subjects than in control subject, although no statistical analysis was reported on the observed data. In comparison, the subjects managed with medical treatment showed no improvement in hair pull test or hair growth.

Multiple preliminary and observational studies performed in 2014 all concluded that PRP could have a positive therapeutic effect for male and female subjects with AGA. Schiavone et al[20] led an observational study in which 64 subjects received 2 injections of L-PRP mixed with plasmatic proteins 3 months apart. Hair count and thickness were visibly improved after 6 months of PRP treatment; approximately 40.6% of study participants reached at least a moderate level of improvement.

Gkini et al[21] performed a prospective cohort study with 22 subjects, of which 20 completed the study. After 3 treatments, they reported increased hair density compared to baseline at 3, 6, and 12 months after PRP ($p < 0.001$), as well as improvements in density and thickness. Investigators also suggested that the PRP treatment appeared to lead to increases in hair diameter more than hair count.

Khatu et al[22] also led a small prospective cohort study to investigate PRP efficacy in 11 subjects. After 4 sessions of PRP, 9 subjects reverted to having a negative hair pull test. Hair volume, coverage and follicular hair unit count were improved. Hair counts were noted to be increased from 71 to 93.09 on average. Significant reduction in hair loss was evident per patient questionnaires. Both Gkini et al[21] and Khatu et al[22] assessed patient satisfaction, and found the reported means of 7.1 and 7.0 out of 10, respectively.

After careful evaluation of the clinical outcome and review of previous investigations cited, the available evidence suggests a promising use for PRP as an alternative treatment for AGA. There were no major adverse effects in present study.

Conclusions:

Present study concluded an effective response and relative safety for the application of PRP in the treatment of AGA. PRP associated with hair growth and improve the subject's satisfaction. Thus, PRP can be considered a standard treatment protocol, especially for those patients with negative response to the other treatment or topical use of minoxidil.

References:

1. Cervantes J, Perper M, Wong LL, et al. Effectiveness of Platelet-Rich Plasma for Androgenetic Alopecia: A Review of the Literature. Skin Appendage Disord. 2018;4(1):1-11.
2. McElwee KJ, Shapiro JS. Promising therapies for treating and/or preventing androgenic alopecia. Skin Therapy Lett. 2012;17:1–4.
3. Agarwal S, Godse K, Mahajan A, Patil S, Nadkarni N. Application of the basic and specific classification on patterned hair loss in Indians. Int J Trichology. 2013;5:126–131.
4. Gupta M, Mysore V. Classifications of patterned hair loss: a review. J Cutan Aesthet Surg. 2016;9:3–12
5. Dinh QQ, Sinclair R. Female pattern hair loss: current treatment concepts. Clin Interv Aging. 2007;2:189–199.
6. Olsen EA. ed 2. New York: McGraw-Hill; 2003. Disorders of Hair Growth: Diagnosis and Treatment.
7. Adil A, Godwin M.The effectiveness of treatments for androgenetic alopecia: a systematic review and meta-analysis J Am Acad Dermatol 2017 Jul;77(1):136-141.e5.
8. Singhal P, Agarwal S, Dhot PS, Sayal SK. Efficacy of platelet-rich plasma in treatment of androgenic alopecia. Asian J Transfus Sci. 2015;9:159–162.
9. Marwah M, Godse K, Patil S, Nadkarni N. Is there sufficient research data to use platelet-rich plasma in dermatology? Int J Trichology. 2014;6:35–36.
10. Dhillon RS, Schwarz EM, Maloney MD. Platelet-rich plasma therapy – future or trend? Arthritis Res Ther. 2012;14:219.
11. Ahmed S, Abushaikha S. Platelet-Rich Plasma for Androgenetic Alopecia in Women: A Single-Center Case Series Study in Qatar. International Journal of Dermatology and Venereology 2020; 3(4): 228-230
12. Giordano S, Romeo M, di Summa P, Salval A, Lankinen P. A Meta-analysis On Evidence Of Platelet-rich Plasma for Androgenetic Alopecia. Int J Trichology. 2018;10(1):1-10.
13. Boswell SG, Cole BJ, Sundman EA, Karas V, Fortier LA. Platelet-rich plasma: a milieu of bioactive factors. Arthroscopy. 2012;28:429–439.
14. Akiyama M, Smith LT, Holbrook KA. Growth factor and growth factor receptor localization in the hair follicle bulge and associated tissue in human fetus. J Invest Dermatol. 1996;106:391–396.
15. Cervelli V, Garcovich S, Bielli A, Cervelli G, Curcio BC, Scioli MG, Orlandi A, Gentile P. The effect of autologous activated platelet rich plasma (AA-PRP) injection on pattern hair loss: clinical and histomorphometric evaluation. Biomed Res Int. 2014;2014:760709
16. Zhou S, Qi F, Gong Y, Zhang C, Zhao S, Yang X and He Y. Platelet-Rich Plasma in Female Androgenic Alopecia: A Comprehensive Systematic Review and Meta-Analysis. Front. Pharmacol. 2021; 12:642980.
17. Anitua E, Pino A, Martinez N, Orive G, Berridi D. The effect of plasma rich in growth factors on pattern hair loss: a pilot study. Dermatol Surg. 2017;43:658–670.
18. Alves R, Grimalt R. Randomized placebo-controlled, double-blind, half-head study to assess the efficacy of platelet-rich plasma on the treatment of androgenetic alopecia. Dermatol Surg. 2016;42:491–497
19. 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;4:1317–1323.
20. Schiavone G, Raskovic D, Greco J, Abeni D. Platelet-rich plasma for androgenetic alopecia: a pilot study. Dermatol Surg. 2014;40:1010–1019
21. Gkini M-A, Kouskoukis A-E, Tripsianis G, Rigopoulos D, Kouskoukis K. Study of platelet-rich plasma injections in the treatment of androgenetic alopecia through a one-year period. J Cutan Aesthet Surg. 2014;7:213–219
22. Khatu SS, More YE, Gokhale NR, Chavhan DC, Bendsure N. Platelet-rich plasma in androgenic alopecia: myth or an effective tool. J Cutan Aesthet Surg. 2014;7:107–110