Effectiveness of Platelet-Rich Plasma in the Treatment of Androgenetic Alopecia - A Prospective Cohort Study from Guntur, Andhra Pradesh

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ABSTRACT

BACKGROUND

Androgenetic alopecia (AGA) is a genetically determined disorder characterized by the gradual conversion of terminal hairs into indeterminate, and finally into vellus hairs. It is the most common cause of hair loss affecting more men and occasionally women. Platelet-rich plasma (PRP) therapy is one of the newer treatment options and has shown promising results. We wanted to evaluate the safety and efficacy of PRP in the treatment of AGA.

METHODS

A prospective cohort study was done on thirty patients of AGA. The stage of alopecia was evaluated according to the Hamilton-Norwood scale (males) and the Ludwig scale (females). All patients were treated with six intradermal PRP sittings with an interval of 4 weeks between each sitting and were evaluated at the end of 6 months using global photography, hair pull test, patient's satisfaction rating and hair density.

RESULTS

Out of 30 patients, majority were in the age group of 21 - 25 years (40 %)**.** 23 were males and 7 were females. Among male patients, maximum number of patients (39.13 %) were having grade 4 AGA followed by grade 3 (30.43 %). Among females, maximum number of patients (57.14 %) were having grade 1 AGA. At baseline, 66.67 % patients showed positive hair pull test whereas all patients showed negative hair pull test at the end of study. Baseline mean hair density was 78.96 ± 9.66 hairs / cm^2 and at the end of study it was 105. 46 ± 9.21 hairs / cm^2. On an analogue scale ranging from 0 to 10, the overall mean change in the clinical rating of patient satisfaction was 6.83, which denoted satisfactory for most patients.

CONCLUSIONS

All patients treated with PRP showed increase in hair density in dermoscopic photomicrographs at the end of the study. PRP is a simple, effective and safe treatment for AGA.

KEYWORDS

Androgenetic Alopecia, Platelet-Rich Plasma

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BACKGROUND

Androgenetic alopecia (AGA) is a hereditary, androgen-dependent progressive thinning and loss of the scalp hair in a specifically defined pattern which is a common dermatological disorder affecting more men and occasionally women with a significant negative impact on their social and psychological well-being.[1]

In India, a population-based study showed a prevalence of 58 % in males aged between 30 to 50 years.[2] It commonly begins by 20 years of age and affects nearly 50 % of men by the age of 50 years.[1] Its frequency increases with age, even though it may start at puberty. The FDA approved drugs for AGA, like minoxidil and finasteride, are associated with side effects like a headache, an increase in unwanted hair and loss of libido respectively and requires a long-term treatment affecting the patient's compliance and surgical management includes hair restoration procedures like hair transplantation which is a costly procedure. This prompted us to evaluate the efficacy and safety of the Platelet-rich plasma (PRP) in the treatment of AGA.

PRP has been used in many medical and surgical specialties in the past to prevent infection and speed up the wound healing process. PRP is an autologous concentration of human platelets in a small volume of plasma that has a higher platelet concentration (4 - 7 times) above the baseline. The proposed mechanism of action of PRP is attributed to the various growth factors that are released from the platelets acting on stem cells in the bulge area of the hair follicles, stimulating the growth and development of new follicles and promoting angiogenesis.[3]

The optimal concentration of platelets is the single most important factor in determining the efficacy of PRP in the treatment of AGA.[4] In this study, we have standardized the method of PRP preparation by using a centrifuge and other parameters were also maintained to obtain maximal platelet concentration in PRP so that we can evaluate the efficacy and safety of PRP in the treatment of AGA.

We wanted to evaluate the safety and efficacy of Platelet Rich Plasma in the treatment of androgenetic alopecia.

METHODS

This is a prospective cohort study. Thirty clinically diagnosed patients of androgenetic alopecia attending Department of Dermatology, Venereology and Leprosy OPD at NRI Medical College and General Hospital, Chinakakani, Guntur were enrolled in this study. The study was done for 18 months' period from January 2019 till June 2020 after getting approval from institutional ethics committee. The procedure and purpose of this study was explained to all patients and written informed consent was obtained.

Procedure

Diagnosis of Androgenetic alopecia in all patients was made based on detailed history (any drugs causing hair loss), clinical examination, and laboratory tests. In our study, we evaluated hair loss, the mean increase in the number of hair, patient satisfaction and side effects.

Laboratory Tests Included (If Necessary)

1. Complete blood count (CBC)
2. Serum iron, serum ferritin, total iron-binding capacity
3. Folic acid
4. T 3, T 4, Thyroid stimulating hormone (TSH), Anti-thyroid peroxidase (ANTI – TPO) antibodies, FT 3, FT 4
5. VDRL

Laboratory tests were done to exclude other hair loss causes, such as anaemia, poor nutrition and thyroid dysfunction.

Evaluation Methods Included

1. Hair pull test
2. Dermoscopic photomicrographs
3. Global photographs
4. Patient's satisfaction rating based on a linear analogue scale is used for measuring patient's satisfaction. It is a linear scale ranging from 0 to 10.
    - 0 = Very Dissatisfied
    - 1 to 4 = Dissatisfied
    - 5 = no change
    - 6 to 9 = Satisfied
    - 10 = Very Satisfied.

Inclusion Criteria

Male Patients with androgenetic alopecia stage II - VII Hamilton-Norwood classification and Female Patients with androgenetic alopecia stage I - III Ludwig scale were included in our study.

Exclusion Criteria

- Our Exclusion Criteria included Patients with alopecia other than androgenetic alopecia, Patients with a history of bleeding disorders or on anticoagulant medications (aspirin, warfarin, heparin) or active local infection, keloidal tendency, history of psoriasis or lichen planus because of the risk of the Koebner phenomenon, Patients with chronic illness, patients who have undergone any form of treatment (at least in past 3 months) and patients not willing to participate in the study.
- Known patients of HIV, hepatitis B or C positive or otherwise immunocompromised are also excluded from our study.

Autologous PRP Preparation Method

- PRP is prepared by Syringe Only Technique by collecting 34 ml of venous blood and mixed with 6ml of Acid Citrate Dextrose solution (ACD-A) in disposable syringes under proper aseptic precautions. To avoid any unintentional activation of platelets, large bore needles of size 22 G were used to draw the blood.
- The syringes were rotated in a centrifugation machine at 1500 revolutions per minute for 15 minutes. The first

centrifugation is called "soft spin.

- The supernatant plasma containing platelets is transferred into another sterile syringe without anticoagulant using a 3 - way connector.
- This syringe underwent second centrifugation, which was shorter and faster than the first, called "hard spin," comprising of 3500 revolutions per minute for 7 minutes. It allows the platelets to settle as a pellet at the bottom of the tube from platelet-poor plasma (PPP) above.
- Approximately 2 / 3rd of the supernatant PPP is discarded, and the platelet-rich pellet is re suspended in the remaining amount of plasma. It was loaded in insulin syringes.
- PRP was injected into the intradermal tissue in a dose of 0.05 - 0.1 ml / cm 2 (2 - 4 insulin units) at the affected site. A vibrating device is placed adjacent to the injection site to decrease the injection pain.
- Six such treatments with an interval of 4 weeks throughout six months were given.
- Evaluation methods included Hair pull test, Global photographs, Patient satisfaction rating based on a linear analogue scale was recorded.
- Evaluation of patients done at – T 1 at the beginning of the study, T 2 is 1 month after 1st session, T 3 is 1 month after 2nd session, T4 is 1 month after 3rd session, T 5 is 1 month after 4th session, T6 is 1 month after 5th session, and T 7 is 1 month after 6th session which is at the end of the study.

Ethical Considerations

The study was approved by the instituitional human ethics committee (Ref: NRIAS / IEC / 439 / 2018). Informed written consent was obtained from all study participants. Confidentiality of the study participants was maintained throughout the study.

Statistical Analysis

Quantitative variables were analysed by mean ± standard deviation using an advanced statistical software (MedCalc – software version 19.2.6) and paired t-test was applied. $P < 0.05$ was considered as statistically significant.

RESULTS

In this study, majority of patients were in the age group of 21 - 25 years (40 %), followed by 26 - 30 years (23.33 %). The age of the youngest patient was 20 years and that of the oldest was 43 years. The mean age of the patients was 27.23 years. Out of 30 patients, 23 (76.67 %) were males and 7 (23.33 %) were females. Out of 23 male patients in the study, maximum number of patients (39.13 %) were having grade 4 AGA, according to Norwood-Hamilton classification, followed by grade 3 (30.43 %) and very few in grade 2 (13.04 %). Among 7 female patients, maximum number of patients (57.14 %) were having grade 1 AGA, according to Ludwig scale and only one patient (14.29 %) presented with grade 3. (Table 1)

At T1, the average number of hairs pulled was 6.23, which reduced to 5.23, 4.23, 2.70, 2.20, 1.76, and 1.23 at T2, T3, T4, T5, T6, and T7 respectively. The hair pull test became negative in all patients at T4 with only 1 patient (3.33 %) showing a positive hair pull test at T5. (Table 2).

	Scales	Number of Patients	Percentage (N=23)
Norwood Hamilton Scale	Grade 2	3	13.04 %
	Grade 3	7	30.43 %
	Grade 4	9	39.13 %
	Grade 5	4	17.40 %
Ludwig Scale	Grade 1	4	57.14 %
	Grade 2	2	28.57 %
	Grade 3	1	14.29 %

Table 1. Grading of Patients According to Norwood Hamilton Scale and Ludwig Scale

Time of Observation	The Mean No. of Hairs Pulled during the Test	Percentage of Patients Positive for a Hair Pull Test
T1	6.23	66.67 %
T2	5.23	43.33 %
T3	4.23	20.00 %
T4	2.70	0.00 %
T5	2.20	3.33 %
T6	1.76	0.00 %
T7	1.23	0.00 %

Table 2. Percentage of Patients Positive for a Hair Pull Test

Time of Observation	Hair Density	Percentage Increase in Hair Density from Baseline
T1	78.96 ± 9.66	–
T2	80.83 ± 9.43	2.36 %
T3	85.70 ± 9.95	8.53 %
T4	91.40 ± 10.20	15.75 %
T5	96.56 ± 10.00	22.28 %
T6	101.03 ± 9.76	27.95 %
T7	105.46 ± 9.21	33.56 %

Table 3. Percentage Increase in Hair Density from Baseline

Grade of AGA	Mean Hair Density (before)	Mean Hair Density (After 6 Sittings)
Ludwig 1	88.75 ± 11.23	110 ± 8.16
Ludwig 2	87.5 ± 2.12	106.5 ± 0.70
Ludwig 3	83 ± 0	100 ± 0
Norwood Hamilton 2	84.66 ± 4.04	109.33 ± 2.08
Norwood Hamilton 3	81.42 ± 4.68	106.57 ± 3.69
Norwood Hamilton 4	76.22 ± 4.49	100.11 ± 3.21
Norwood Hamilton 5	61.5 ± 2.88	84.25 ± 8.26

Table 4. Comparison of Mean Hair Density Before and After Treatment

Figure 1. Before Starting Treatment and After 6 Sittings of PRP Treatments

Hair density has significantly increased in all patients at T4 (91.40 ± 10.20), T5 (96.56 ± 10.00), T6 (101.03 ± 9.76) and at T7 (105.46 ± 9.21) with a P - value of < 0.001 which was statistically significant, compared to T1, with test statistic t- value of 26.54 and degree of freedom of 29. The percentage increase of hair density was 15.75 %, 22.28 %, 27.95 %, 33.56 % at T4, T5, T6, and T7 respectively compared to baseline values (Table 3). Patients with early grades of AGA showed more improvement compared with patients of higher grades of AGA. (Table 4). Mean hair density before and after 6 sittings showed a P value less than < 0.001, which was statistically significant. On a linear analogue scale ranging from 0 to 10, the overall mean change in the clinical rating of patient satisfaction was 6.83 which denotes satisfaction for most patients.

Side Effects

During the administration of PRP injection, majority of the patients reported only very mild pain on the application of a vibratory device and few patients reported moderate pain. All patients had pinpoint bleeding at a few injection sites and erythema. After the procedure, 50 percent of the patients reported mild pain for 1 - 2 hours and all the patients reported scalp sensitivity during the first hair wash at 24 hours post procedure and this gradually subsided thereafter.

DISCUSSION

Hair represents an important aspect of an individual's self-image and affects social perceptions about that individual.[5] Androgenetic alopecia is a type of progressive patterned hair loss where there is an androgen-mediated conversion of susceptible terminal hairs into vellus hairs in genetically predisposed individuals.[6] Hair loss caused by androgenetic alopecia is also known to affect the psychological well-being of an individual, but local data in this context is lacking.[5] The US Food and Drug Administration (FDA) approved drugs for the management of AGA are topical minoxidil and oral finasteride.[7] Minoxidil appears to prolong the anagen phase and promote the survival of dermal papilla cells and increase in hair follicle size.[8,9] Finasteride also promotes hair growth of anagen hairs leading to a gradual increase in hair diameter and hair elongation[10] and appears to activate anagen hair growth.[11,12]

Various other treatments have been tried besides FDA-approved options.[7] Most of the existing treatment options are relatively slow to act because of which there has been a continuous search for the newer modality of treatment, among which platelet rich plasma therapy is one of them. PRP is an autologous preparation of platelets in concentrated plasma. Platelet rich plasma contains a large array of growth factors such as platelet derived growth factors, vascular endothelial growth factors, epidermal growth factors, fibroblast growth factor 2 and insulin like growth factors which promote hair growth by inducing the follicular stem cells to shift from a dormant to an active state. Vascular endothelial growth factor 8 and platelet derived growth factor 4 also facilitate angiogenesis around the hair follicle.

In AGA, PRP seems to induce differentiation of stem cells, prolongs the survival of dermal papilla cells, prolongs the anagen phase of the hair cycle and increases perifollicular vascular plexus by multiple mechanisms through various GFs. This prompted us to evaluate the efficacy and safety of the PRP in the treatment of AGA.

In the present study, the age group of the patients ranged from 20 – 43 years. The mean age of the patients was 27.23 ± 6.30 years. A maximum number of patients were in the age group of 21 - 25 years (40 %), followed by 26 - 30 years (23.33 %), 36 - 40 years (13.33 %), 20 years (10.00 %). Only one patient (3.33 %) presented in the age group between 41 - 45 years. Patient with minimum age in our study was 20 years, and patient with maximum age was 43 years. In a non-randomized trial to determine the efficacy of PRP, Gkini et al.[13] performed PRP in 20 patients affected by androgenetic alopecia. In their study, the mean age of patients was 34 years. The lesser mean age of presentation signifies that AGA in young individuals has a significant social, psychological impact, and also increasing number of younger individuals are willing to correct their baldness at early presentation.

In the present study, out of 23 males, according to the Hamilton-Norwood scale, a maximum number of patients were in grade 4 (39.13 %), followed by grade 3 (30.43 %), and least in grade 2 (31.04 %). In the present study, out of 7 females, according to the Ludwig scale, a maximum number of patients were in grade 1(57.14 %), followed by grade 2 (28.57 %), and only one patient in grade 3 (14.29 %). Gkini et al.[13] in their study, reported that among men, the maximum number of patients were in Norwood Hamilton grade 3 followed by grade 2. In females, according to the Ludwig scale, one patient suffered from grade 1 and another from grade 3 AGA.

In this study, PRP injections were performed in six treatment sessions. The percentage increase of hair density was 15.75 %, 22.28 %, 27.95 %, and 33.56 % at T 4, T 5, T 6, and T 7, respectively, compared to baseline, i.e., T 1, with a P value less than 0.001. Gkini et al..[13] conducted a nonrandomized prospective cohort study in which they injected PRP in 20 patients as three treatment sessions with an interval of 3 weeks. At six months from the beginning of the treatment, a booster session was also performed. The patient's hair density significantly increased at 6 weeks (154.80 ± 34.39 hairs per cm^2), at 3 months (170.70 ± 37.81 hairs per cm^2). At 6 months, hair density was 156.23 ± 37.75 hairs per cm^2, and at 1 - year hair density was 153.70 ± 39.92 hairs per cm^2 compared with the onset of therapy (P < . 001). Swapna S Khatu[14]et al. reported that in their study where they had given 4 PRP injections at 15 days interval, the average hair density before treatment was 71 hairs / cm^2, which increased to 93.09 hairs / cm^2 at the completion of treatment sessions. The average mean gain was 22.09 hairs / cm^2. There was a 31.11 % increase in hair density compared to the baseline. The percentage increase in hair density in the present study is consistent with the study conducted by Swapna S Khatu et al. The difference in results of Gkini et al. from the present study may be due to:

1. The difference in the total number of treatment sessions.
2. The difference in the duration between treatment sessions.
3. Differences in grades of alopecia in the studies.
4. The protocol used for the preparation of PRP.
5. The type of anticoagulant used for preparing PRP.
6. The endpoints of observation of studies were different.

In the present study, all patients showed good improvement in hair density compared to baseline hair density. Among male patients in the present study, patients with Norwood Hamilton grade 2 showed a mean increase of 24.67 hairs, whereas patients with Norwood Hamilton grade 5 showed a mean increase of 22.75 hairs. Similarly, among the female patients in the present study, patients with Ludwig scale grade 1 showed a mean increase of 21.25 hairs, whereas patients with Ludwig scale grade 3 showed a mean increase of 17 hairs. It signifies that lower grades of alopecia showed more improvement than that of higher grades of alopecia.

In this study, the least number of hairs pulled was at T7. The hair pull test was negative in all the patients in T4, T6 and T7. Only 1 patient had positive hair pull test in T5. Gkini et al.[13]in the study to determine the efficacy of PRP injection in Androgenetic alopecia reported that at the beginning of the study and at three weeks, the hair pull test was positive with a mean of 8 and seven hairs respectively. Hair pull test was negative at 6 weeks, three months, six months, and at one year after the onset of treatment. Swapna S Khatu et al.[14] in their prospective study had a positive hair pull test with a mean number of 10 hair before starting treatment. After 4 treatment sessions 15 days apart, the pull test was negative in 9 patients (81.81 %) with an average number of three hairs. Based on the grading of AGA, different grades of AGA showed different percentage of improvement in hair density compared to baseline. Lower grades of alopecia at baseline showed more improvement than that of higher grades of alopecia.

In this study on a scale of 0 to 10 over an analogue scale, the average patient satisfaction rating was 6.83. Gkini et al.[13] in their study which included 20 patients reported that patients were satisfied with a mean satisfaction rating of 7.1 on a linear analog scale of 1 - 10 (1 = No result, 10 = Best result). Swapna S Khatu et al.[14] reported that in their study patient satisfaction was high with a mean rating of 7.0 on a scale of 1 - 10. Results of patient's satisfaction ratings in the present study were consistent with studies conducted by Gkini et al. and Swapna S Khatu et al.

Gkini et al.[13] reported that during PRP injections, 100 % of them felt mild pain, despite local anesthesia. Parul Singhal et al.[15] reported that in their study only 3 out of 10 patients reported pain after initial administration. Minimal pain, redness, and pinpoint bleeding were the side effects observed by Swapna S Khatuet al.[14]after PRP injections.

CONCLUSIONS

In this study all patients treated with PRP showed some degree of clinical improvement. There was an increase in hair density in dermoscopic photomicrographs at the end of the study. Global photographs also showed a moderate improvement in hair volume and coverage. The visible result was mainly due to increased thickness and / or increased number of hairs rather than an increase in hair length. Early treatment resulted in better outcome. PRP for AGA is a simple, effective, non-surgical and non-scarring procedure with high safety profile and can be considered as a valuable adjuvant treatment modality.

Limitations of the Study

The present study is not a randomized, double-blind, controlled trial. There are no control cases.Trichogram hair evaluation could have given more objective results. The sample size was small, even though the present study had statistically significant results. The mean follow up period was short to evaluate the long-term effectiveness of treatment.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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