Original Research Article

A STUDY OF EFFECTIVENESS OF PLATELET RICH PLASMA IN TREATMENT OF ANDROGENETIC ALOPECIA IN MALES

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Abstract

Background: Aim: A study of effectiveness of platelet rich plasma in treatment of androgenetic alopecia in males. **Materials and Methods:** Patients willing for the procedure, Male patients in the age group of 19-49 years, Patients with androgenetic alopecia stage III-VII Hamilton-Norwood classification and Patients who have not under any form of treatment, at least in the past six months were included in the study. Diagnosis of Androgenetic alopecia in all patients was done based on detailed history (any drugs causing hair loss), clinical examination and laboratory tests. Laboratory tests included: CBC, Serum iron, Serum ferritin, total iron binding capacity, Folic acid, T3, T4, TSH, ANTI-TPO antibodies, fT3, fT4 and VDRL. Laboratory tests were done to exclude other hair loss causes, such as anemia, poor nutrition, thyroid dysfunction, syphilis which may cause syphilitic alopecia. The stage of alopecia was evaluated according to the Hamilton-Norwood scale. **Results:** At T1 the average number of hairs pulled were 10.36, which reduced to 4.9,3.86,3.13 and 5.9 at T3, T4, T5, T6 respectively. The least number of hair pulled was at T5. The percentage reduction of hair pull test from T1 to T6 was 43.05%. Hair density was significantly increased at T3 (83.93±11.84), T4 (87.16 ± 15.23), T5 (104.1 ± 14.02) and T6 (80.5±13.89) with a p-value of 0.01(statistically significant) compared to the onset of therapy (T1) with t-value of -6.426 & degree of freedom of 29 with correlation coefficient of +0.864. Hair density reached its peak at T5. The percentage increase of hair density was 16.19%,20.67%, 44.12%, 11.44% at T3, T4, T5, T6 respectively compared to the onset of therapy. On a scale ranging from -7 to +7 the overall mean change in the clinical rating of patient satisfaction was 4.7. During the administration of PRP injection, all the patients reported mild pain despite local anesthesia and some had pinpoint bleeding and erythema. After the procedure, 20% reported mild pain for 6 hours after the injection.70% of the patients reported scalp sensitivity during first hair wash after the procedure. After six months from the first treatment session, 23 patients (76.7%) showed a mean increase in hair density compared to baseline. Seven patients (23.3 %) showed progressive hair loss leading to a mean decrease in hair loss when compared to T5 but above baseline. **Conclusion:** Non-invasive methods for evaluation like Dermascopic photomicrographs and Global photographs were used and there was an increase hair density in Dermascopic photomicrographs at 3 months interval but decreased during follow up at 6 months but it remained significantly higher than that of baseline i.e. it followed an upward curve reached peak at the end of 3 months and decreased towards the end of 6 months.

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International Journal of Academic Medicine and Pharmacy (www.academicmed.org)
ISSN (O): 2687-5365; ISSN (P): 2753-6556

INTRODUCTION

Androgenetic alopecia (AGA) is a hereditary, androgen-dependent progressive thinning and loss of the scalp hair in a specifically defined pattern, is a common dermatological disorder affecting more men and occasionally in women, with a significant negative impact on their social and psychological well-being.[1] Independent of age and gender, patients diagnosed with AGA may undergo significant impairment of quality of life affecting self-esteem and may lead even to depression and other negative effects on life.[2] Androgenetic alopecia can affect all races, but the prevalence rate varies. In India, a population-based study showed a prevalence of 58% in males aged between 30-50years.[3] 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, increase in unwanted hair and loss of libido respectively and require a long-term treatment affecting the patient's compliance and surgical management include hair restoration procedures like hair transplantation 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 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.[4] The optimal concentration of platelets is the single most important factor in determining the efficacy of PRP in the treatment of AGA.[5] In this study, I 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.

MATERIALS AND METHODS

Thirty clinically diagnosed patients of androgenetic alopecia attending the Department of Dermatology, Venereology, Leprosy OPD at Government General Hospital, Vijayawada, were enrolled based on the inclusion and exclusion criteria. It was a Prospective study conducted from January 2017 – June 2018. Patients willing for the procedure, Male patients in the age group of 19-49 years, Patients with androgenetic alopecia stage III-VII Hamilton-Norwood classification and Patients who have not under any form of treatment, at least in the past six months were included in the study. Patients with alopecia other than androgenetic alopecia, such as alopecia areata, alopecia totalis, telogen effluvium, anagen effluvium, acquired cicatricial alopecia, etc, Patients with a history of bleeding disorders, Patients on anti-coagulant medications (aspirin, warfarin, heparin), Patients with active local infection, Patients with a keloidal tendency, Patients with a history of psoriasis or lichen planus because of the risk of the Koebner phenomenon, Patients with chronic illness, Un-cooperative patients, patients who are unable to understand the protocol or give informed consent, known patients of HIV, hepatitis B or C positive or otherwise immunocompromised were excluded from this study.

Diagnosis of Androgenetic alopecia in all patients was done based on detailed history (any drugs causing hair loss), clinical examination and laboratory tests. Laboratory tests included:

1. CBC
2. Serum iron, Serum ferritin, total iron binding capacity
3. Folic acid
4. T3, T4, TSH, ANTI-TPO antibodies, fT3, fT4
5. VDRL

Laboratory tests were done to exclude other hair loss causes, such as anemia, poor nutrition, thyroid dysfunction, syphilis which may cause syphilitic alopecia. The stage of alopecia was evaluated according to the Hamilton-Norwood scale.
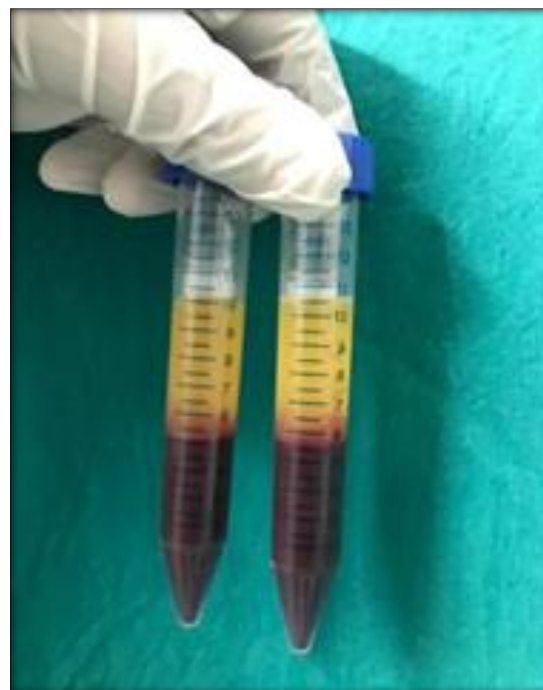
RESULTS

Figure 1: After first centrifugation

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International Journal of Academic Medicine and Pharmacy (www.academicmed.org)
ISSN (O): 2687-5365; ISSN (P): 2753-6556

Figure 2: Platelet pellet formed after second spin

Figure 3: PRP before injecting

Figure 4: 30yr old patient before starting treatment

Figure 5: The Same Patient at 3 Months Following the Onset of PRP Treatment

Figure 6: Male, 30-Year-Old, Before Treatment

Figure 7: The Same Patient After 4 Sessions of PRP Treatment

Figure 8: 22-Year-Old Male Patient Before Starting PRP

Figure 9: Same Patient at The End of 6 Months

Figure 10: Same patient before PRP treatment

Figure 11: Same patient after 6 months from baseline

Figure 12: Male, 36-year-old, before treatment

Figure 13: The same patient at 3 months following the onset of PRP treatment

Majority of patients were in the age group of 31-35 years (30%), followed by 36-40 years (26.66%). The age of the youngest patient was 20 years, and that of the oldest was 40 years. The mean age of the patients was 31 years. [Table 1]

Out of 30 male patients in the study, a maximum number of patients were in grade 3 of AGA according to Norwood-Hamilton classification (43.33%), followed by grade 4 (36.66%) and lowest in grade 5 (10%). [Table 2]

At T1 the average number of hairs pulled were 10.36, which reduced to 4.9, 3.86, 3.13 and 5.9 at T3, T4, T5, T6 respectively. The least number of hair pulled was at T5.

The percentage reduction of hair pull test from T1 to T6 was 43.05%. [Table 3]

Hair density was significantly increased at T3 (83.93±11.84), T4 (87.16 ± 15.23), T5 (104.1 ± 14.02) and T6 (80.5±13.89) with a p-value of 0.01(statistically significant) compared to the onset of therapy (T1) with t-value of -6.426 & degree of freedom of 29 with correlation coefficient of +0.864. Hair density reached its peak at T5. The percentage increase of hair density was 16.19%, 20.67%, 44.12%, 11.44% at T3, T4, T5, T6 respectively compared to the onset of therapy.

On a scale ranging from -7 to +7 the overall mean change in the clinical rating of patient satisfaction was 4.7. During the administration of PRP injection, all the patients reported mild pain despite local anesthesia and some had pinpoint bleeding and erythema. After the procedure, 20% reported mild pain for 6 hours after the injection. 70% of the patients reported scalp sensitivity during first hair wash after the procedure. After six months from the first treatment session, 23 patients (76.7%) showed a mean increase in hair density compared to baseline. Seven patients (23.3 %) showed progressive hair loss leading to a mean decrease in hair loss when compared to T5 but above baseline. [Table 4].

Table 1: Age Distribution of Patients

Age interval (years)	Number of patients	Percentage
19-20	01	3%
21-25	04	13.33%
26-30	07	23.33%
31-35	10	30%
36-40	08	26.66%

Table 2: Grading of Male Patients According to Norwood- Hamilton Classification

Grade of AGA	Number of patients	Percentage
III	13	43.33%
IV	11	36.66%
V	6	20%

Table 3: Hair Pull Test

Time of observation	Percentage of patients positive for a hair pull test	The mean number of hairs pulled during hair pull test	Percentage reduction of hairs pulled during hair pulled test at the end of treatment from baseline
T1	100%	10.36	_
T2	100%	10.36	_
T3	13.33%	4.9	55.59%
T4	6.66%	3.86	62.74%
T5	3.33%	3.13	69.79%
T6	20%	5.9	43.05%

Table 4: Hair Density

TIME POINTS	HAIR DENSITY
T1	72.23 ± 11.24
T2	72.23 ± 11.24
T3	83.93 ± 11.84
T4	87.16 ± 15.23
T5	104.1 ± 14.02
T6	80.5 ± 13.89

DISCUSSION

Androgenetic alopecia remains the most common hair loss disorder with significant impact on the social and psychological well being. Since Androgenetic alopecia is characterized by miniaturization of the terminal to vellus hair, and a shortened anagen phase. 6current therapeutic strategies target cellular proliferation and differentiation during the hair cycle. Except for scalp surgery, finasteride and minoxidil are the only FDA-approved pharmacological therapies.[6,7,8] Minoxidil appears to prolong anagen phase and to promote 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 61 and appears to activate anagen hair growth.[11,12] Activated PRP seems to promote differentiation of stem cells into hair follicle cells through the upregulation of transcriptional activity of β-catenin. It also induces in vitro proliferation of dermal papilla cells and increases dermal papilla cell growth by activating ERK signaling. Li et al. performed an in vivo study, where mice received subcutaneous injections of PRP, and their results were equated with control mice. Activated PRP increased the proliferation of dermal papilla (DP) cells and stimulated extracellular signal-regulated kinase and Akt signaling. Fibroblast growth factor 7 (FGF-7) and beta-catenin, both potent stimuli of hair growth were upregulated in the DP cells. The injection of mice with PRP induced faster telogen-to-anagen shift than that was seen in control mice.[13] Therefore the present study tried to evaluate the efficacy and safety of PRP in the treatment of AGA.

In the present study, age group of the patients ranged from 19 – 49 years. The average age of the patients was 31 years. A maximum number of patients were in the age group of 31-35 years (30%), followed by 36-40 years (26.66%), 26-30 years (23.33%), 21-25 years (13.33%), 19-20 years (3%). Gupta et al14 reported that maximum number of patients were in the age group 25 to 35 and mean age group was 28.3 ± 3.1 years. Mean age group in the present study was consistent with studies conducted by Gupta et al.[14]

This shows that AGA has a significant social and psychological impact on young individuals.

In the present study, out of 30 male patients according to the Hamilton-Norwood scale, a maximum number of patients were in grade 3(43.33%), followed by grade 4 (36.66%), and least in grade 5 (20%). In a study conducted by Gupta et al14 maximum number of patients were in grade 6 followed by grade 5, grade 3 and grade 4. Gkini et al15 in their study reported that among men, according to the Hamilton- Norwood scale, the maximum number of patients were in grade 3, followed by grade 2, 4, 5 in decreasing order which

is close to our study. In females, according to Ludwigs scale, one patient suffered from grade 1 and another from grade 3 AGA. The maximum number of patients in present study belonged to grade III at which it is visually more apparent to the patient when compared to grade I and grade II and intervention at this stage could show better results. [Table 5]

In the present study, at T1 the average number of hairs pulled were 10.36, which reduced to 3.86, 3.13, 4.9, 5.9 at T3, T4, T5, T6 respectively. The least number of hair pulled was at T4. The percentage reduction of hair pull test from T1 to T6 was 43.06%. Hair pull test was negative in all the patients at the end of the treatment session. Parul Singhal et al,[18] administered autologous PRP injections thrice with an interval of 2-3 weeks; they reported that hair pull test reduced by an average of 65% at the end of their study Swapna S Khatu et al,[17] in their prospective study which studied the efficacy and safety of PRP in AGA gave 4 PRP injections at 15 days interval reported that all the patients (had a positive hair pull test with a mean number of 10 hair before starting treatment. After all the treatment sessions, the pull test was negative in 9 patients (81.81%) with an average number of three hairs. [Table 6]

In present study cessation of hair fall seen after two weeks of initiation of treatment with PRP which was much earlier when compared to minoxidil or finasteride therapy which may be due to direct delivery of Growth factors at the level of dermis where hair follicles are present. In the present study, hair density was significantly increased at T3 (83.93±11.84), T4 (87.16±15.23), T5 (104.1±14.02) and T6 (80.5±13.89) with a p-value of less than 0.01(statistically significant) compared to the onset of therapy (T1). Hair density reached its peak at T5. The percentage increase of hair density was 16.19%, 20.67%, 44.12%, and 11.44% at T3, T4, T5, and T6 respectively compared to baseline. At six months from the beginning of the treatment, a booster session was also performed. The patients presented hair density significantly increased at 6 weeks (154.80 ± 34.39 hairs per cm2), at 3 months (170.70 ± 37.81 hairs per cm2), at 6 months (156.23 ± 37.75 hairs per cm2), and at 1 year (153.70 ± 39.92 hairs per cm2) compared with the onset of therapy (p < .001). Swapna S Khatu,[17] et al. reported that in their study which gave 4 PRP injections at 15 days interval, before treatment the average hair count over a marked area was 71 hair follicular units which increased to 93.09 follicular units after completion of treatment sessions. The average mean gain is 22.09 follicular units per cm2. There was a 30% increase in hair density compared to the baseline. Pietro Gentile et al,[20] reported that in their study there was a mean increase in total hair density of 45.9 hairs per cm2 when compared with baseline was observed after 3 months, and the control area displayed a mean decrease of 3.8 hairs per cm2) in

hair density at the same time (control vs. treatment: p < .0001). [Table 7]

The results of the present study are for the greatest part in consistent with the results of Gkini et al,[15] and Uebel et al.[4] In Gentile et al. study20, the end point of observation was three months after the first PRP injection, which showed a mean increase in hair density of 45.9 hairs per cm2 which was much higher when compared to the increase of 31.87 ± 2.78 hairs per cm2 at the same point of time in the present study. The difference in results may be due to the different protocols used for the preparation of PRP. In the present study, the overall mean change in clinical rating was 4.7 (a good deal better) according to Jaeschke rating scale 21 in all the patients. [Table 8]

In a study done by Schiavone et al. 22 with 64 patients of androgenic alopecia, the results obtained after two injections of leukocyte platelet-rich plasma (L-PRP) with the addition of concentrated plasmatic proteins, at baseline and after three months. Two independent evaluators assesed them using the Jaeschke rating of clinical change. The mean change in clinical rating was 3.2 (95% confidence interval [CI]: 2.9–3.5) and 3.9 (95% CI: 3.5–4.3), respectively.

Gkini et al,[15] in their study with included 20 patients, reported that patients were satisfied with a mean satisfactory rating of 7.1 on a linear analog scale of 1-10 (1 = no result, 10 = best result). These results were consistent with the present study.

More patient satisfaction rate was achieved with PRP treatment which may be due to immediate and significant results without any long-term side effects and better patient compliance as it is a day care procedure. In the present study during the administration of PRP injection all the patients reported mild pain despite local anesthesia and some had pinpoint bleeding and erythema.

After the procedure, 20% reported mild pain for 6 hours after the injection and 70% of the patients reported scalp sensitivity during first hair wash after the procedure. None of the patients had any infection or inflamation. Gkini et al,[15] reported that during PRP injections 100% of them felt mild pain, despite local anesthesia. After application, 25% of them felt a mild pain feeling, which subsided after 4 hours, while 60% had scalp sensitivity during first hair wash after treatment injections. None reported any worsened hair shedding, infection or ecchymosis. These results were consistent with the present study. Parul Singhal et al,[18] reported that in their study only 3 out of 10 patients reported pain after initial administration. None of the patients had inflammation or infection which was consistent with the present study. The side effects are minimal when compared to other medical and surgical treatment modalities, and hence can be considered as a safe choice of treatment. [Table 9]

In this study, none of the patients presented with decreased hair density at T3 and T4 compared to baseline and only two patients presented with no change (6.66%). At T5, two patients (6.66%) presented a mean decrease of 2 hair/cm2 in hair density compared to that of T1; while at T6, 23.3 % of patients presented a mean decrease of 3.71 hair/cm2 Gkini et al,[15] reported in a nonrandomized trial the efficacy of PRP injection in 20 patients affected by androgenic alopecia. This prospective cohort study was based on 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 study reported that at six weeks and three months, none of the patients presented decreased hair density compared to that of the baseline and only one of them presented no change (5%). At six months, one patient (5%) presented a mean decrease of 1 hair/cm2 in hair density compared to that of the beginning of the study, while at one year 30% presented a mean decrease of 2 hair/cm2. These results were consistent with the present study. [Table 10]

In follow up the period decrease in hair density was seen in 7 patients. [Table 11]

Table 5: Comparison of age-wise distribution of patients with other studies

Studies	The range of age group of patients	Mean age of patients
PRESENT STUDY	19 – 49 years	31years
GUPTA ET AL[14]	25-35 years	28.3±3.1 years
GKINI ET AL[15]	24-72 years	34 years
GULNAR ET AL[16]	21 – 58 years	40.2 years

Table 6: comparison of distribution of patients in various grades of aga in male patients with other studies

Studies	Total number of male patients	% of patients in grade 2	% of patients in grade 3	% of patients in grade 4	% of patients in grade 5	% of patients in grade 6
PRESEN T STUDY	30	-	43.33%	36.66%	20%	-
GUPTA ET AL[14]	30	-	16.66%	13.33%	33.33%	36.66%
GKINI ET AL[15]	18	27.77%	44.44%	22.22%	5.55%	
SWAPNA S KHATU ET AL[17]	11	36.36%	36.36%	27.27%	-	

Table 7: comparison of results of hair pull test with other studies

Studies	Percentage reduction in hairs pulled during hair pull test at the end of treatment from the baseline	Percentage of patients having negative hair pull test at the end of the study
Present Study	43.06%	80%
Parul Singhal Et Al[18]	65%	-
Gkini Et Al15	-	100%
Swapna S Khatu Et Al[17]	-	81.81%
Besti Et Al[19]	-	100%

Table 8: Comparison of results of hair density with other studies

Studies	Hair density at t0	Hair density at te	Statistical significance	Percentage or mean an increase in the number of hair from t0 to te
Present study	72.23 ± 11.24	80.5 ± 13.89	P < 0.0001 statistically significant	11.44%
Gkini et al[15]	143.10 ± 31.07	153.70 ± 39.92	p< .001 statistically significant	7.41%
Swapna s katu et al[17]	71	93.09		30%
Uebel et al[4]	-	-	-	15.1%
Gentile et al[20]	-	-	p< .0001 statistically significant	2 45.9 hairs per cm

Table 9: Comparison of satisfaction rates with other studies

Studies	Satisfaction rates
Present study	4.7 according to the jaeschke scale
Schiavone et al[22]	3.2 and 3.9 respectively according to Jaeschke scale by two independent evaluators
Gkini et al[15]	7.1 / 10 on a linear analog scale
Swapna s khatu et al[17]	7 / 10 on a linear analog scale

Table 10: comparison of side effects of PRP administration with other studies

Studies	Pain	Pin-point bleeding	Erythema at injection site	Scalp sensitivity
PRESENT STUDY	+	+	+	+
GKINI ET AL[15]	+	-	-	+
PARUL SINGHAL ET AL[18]	+	-	-	-
SWAPNA S KATU ET AL[17]	+	-	+	-

Table 11: Comparison of relapse rates with PRP in aga with other studies

Studies	Percentage of patients showing relapse at the end of the study	Mean decrease in the number of hair of the patients showing relapse
Present study	23.3 %	3.71 hair/cm 2
Gkini et al[15]	30%	2 hair/cm 2
Gentile et al[20]	13.33 %	-

CONCLUSION

In this study, we observed that all patients treated with PRP showed some degree of clinical improvement. Non-invasive methods for evaluation like Dermascopic photomicrographs and Global photographs were used and there was an increase hair density in Dermascopic photomicrographs at 3 months interval but decreased during follow up at 6 months but it remained significantly higher than that of baseline i.e. it followed an upward curve reached peak at the end of 3 months and decreased towards the end of 6 months. Even Global photographs showed a moderate improvement in hair volume and coverage. The visible result was mainly due to increased thickness and/ higher number of hairs rather than increase in hair length. PRP for AGA is simple, cost-effective and feasible treatment for hair loss. Considering safety profile and minimal morbidity it can be viewed as a valuable adjuvant treatment modality for AGA.

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International Journal of Academic Medicine and Pharmacy (www.academicmed.org)
ISSN (O): 2687-5365; ISSN (P): 2753-6556