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Efficacy of platelet rich plasma for treatment of Male Androgenetic Alopecia patients: A Prospective Clinical Study

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Abstract

Background:
Androgenetic alopecia (AGA) is the most common cause of hair loss in men. Platelet-rich plasma (PRP) has gained popularity as an effective treatment modality. It is an autologous solution with numerous growth factors that contribute to regeneration of hair. Growth factor concentrate or PRP, formed by the activation of platelets has thus emerged as a new potential therapeutic approach for treatment of AGA.
Objectives:
To evaluate the efficacy of PRP for treatment for Androgenic Alopecia in male patients with topical application of Minoxidil and Non-minoxidil solutions.
To evaluate the level of patient satisfaction after the treatment.
Methodology:
A randomized, physician and evaluator blinded, prospective, interventional study was conducted for 100 male androgenetic alopecia patients aged between 20-50 years who showed Male Patterned Hair Loss (MPHL) from Stage II to IV according Norwood – Hamilton Scale. Randomization was done to allocate the patients into two groups - Group A (PRP with topical Minoxidil solution) and Group B (PRP with topical non-minoxidil solution). Platelet rich plasma was prepared using Follirich kits by Wockhardt. Each patient underwent 3 sessions of PRP treatment at an interval of one month each. Patients were evaluated at baseline and after 6 months by hair pull test, global macrophotography, dermoscopic images and patient self-assessment.
Results:
Our results revealed an improvement in the hair fall and hair pull test, hair density and volume in both the groups. There was high patient satisfaction in both the groups. However, the percentage of dissatisfied or unsure patients was greater in group B.
Conclusion:
Platelet Rich Plasma is an emerging treatment modality for patients with androgenic alopecia. When used along with a minoxidil or non-minoxidil solutions, it results in increased hair volume, density, reduced hairfall and high patient satisfaction. Our study highlights the results of commercialised PRP kits for male AA.

Keywords: Platelet-rich plasma; Androgenic Alopecia; Minoxidil; Male pattern hair loss

INTRODUCTION

Androgenetic alopecia (AGA) or male pattern hair loss is a progressive, non-scarring diffuse alopecia characterized by the progressive miniaturization of hair follicles with a diminished anagen phase. It is accompanied by transformation of healthy terminal hair follicles into vellus-like hairs in androgen-sensitive areas of the scalp.[1-3] The Hamilton-Norwood classification has been the standard system for classifying the stages of androgenic alopecia in males.[4] Current standard treatment options are

limited to topical minoxidil, oral treatments like nutritional supplements and oral finasteride, low level laser therapy and micro needling.[5]

Platelet-rich plasma or Autologous growth factor concentrate treatment is an autologous preparation of platelets in plasma that has been widely used for tissue regeneration in various fields.[6] Role of PRP for hair re-growth was first reported by Uebel et al. in 2006.[7] Studies have revealed that PRP acts by inducing a significant initiation and prolongation of the anagen phase of hair growth. The utility of platelet-rich plasma is mainly rooted in the presence of growth factors in plasma.[6]

It has emerged as a new potential therapeutic approach for treatment of AGA recently. Growth factor concentrate is formed by the activation of platelets which leads to release of various growth factors and cytokines from the alpha granules.[2] Highly specific growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), FGF (fibroblast growth factor), IGF (insulin like growth factor 1), EGF (epidermal growth factor)[2, 8, 9] are believed to promote cell proliferation, differentiation, angiogenesis, and chemotaxis that is required for hair regrowth.[2]

Even though there are various studies on PRP for androgenic alopecia, use of autologous growth factor concentrate along with other treatment modalities has not been extensively studied. In this study, we aimed to evaluate the efficacy of PRP treatment for Androgenic Alopecia male patients with topical application of Minoxidil and Non-minoxidil solutions and also the level of patient satisfaction after the treatment.

MATERIALS AN METHODS

Study Design and Setting:

A randomized, physician and evaluator blinded, prospective, interventional study was conducted at our clinic in New Delhi from September 2020 to March 2021. A total of 100 male patients of androgenetic alopecia aged between 20-50 years who showed MPHL Stage II to IV according Norwood – Hamilton Scale were included in the study (Table 1).

Diagnosis of MPHL was established on the basis of a detailed medical history, family history, clinical examination, and laboratory tests (Complete blood count, Serum Ferritin, Vitamin D3, Vitamin b12, thyroid function tests and viral markers). Laboratory tests were done to eliminate other causes of hair loss such as anemia, nutritional deficiency, thyroid dysfunction.

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Male patient aged 20-50 years	Uncontrolled diabetes, Thyroid dysfunction
MPHL Stage II to IV according to Norwood-Hamilton Scale	Platelet disorders, Anemia, Bleeding disorders
Patients who have not taken any other treatment or any topical or systemic medications for AGA in the last 6 months	HIV, Hepatitis B or C positive or otherwise immunocompromised
	History of malignancies
	Active skin disease or infection at the time of treatment
	Tendency for keloid formation

The study comprised of two groups of 50 patients each – Group A (PRP with topical Minoxidil solution) and Group B (PRP with topical Non-minoxidil solution). The Non- minoxidil solution consisted of redensyl, anagain

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and organic pea sprout extract. Each patient underwent 3 sessions of PRP treatment using Follirich kit by Wockhardt. An online randomization generator was used to allocate patients into the two groups. The physicians involved in the treatment and evaluation of the patient were blinded to treatment allocation, and blinding was maintained till all data was analyzed at the end of the study. The patients were aware of the topical solution they were applying.

Study was done in accordance with Declaration of Helsinki. Patients were explained about the treatment outcome and limitations and written informed consent was taken from all patients prior to the treatment.

Preparation of Bio PRP:

- 14 – 16 ml blood was collected from the medial cubital vein under strict aseptic conditions and distributed equally into four tubes containing platelet activating solution (Follirich kit – Wockhardt).
- Blood was gently mixed by rotating the tubes 6-10 times.
- The tubes were allowed to stand for 30 minutes which allows activation of the platelets (by Wockhardt's platelet activating solution) and release of highly specific growth factors (PDGF, VEGF, IGF-1, EGG).
- Centrifugation is done by single spin at 3400 rpm for 10 minutes to separate the PRP from the remaining components of blood, by using Remi 8-C centrifuge machine.
- Approximately 6-8 ml of autologous solution is collected.

Treatment Protocol:

Three sessions of PRP treatment were done for all patients at an interval of one month. Patients were followed up for a period of 6 months.

Under strict aseptic conditions, area of the scalp to be treated was cleaned with an alcohol swab. PRP was injected using an insulin syringe intradermally over the affected area (frontal, mid crown and crown area) by multiple small injections in a linear pattern (nappage technique). Approximately 6-8 ml of the PRP was injected at $0.1ml/cm^2$. Injection was done by the same physician for all patients.

Assessment Criteria:

Patients were evaluated pre-treatment and after 6 months from the start of treatment. The effects of the treatment were assessed in all patients by physician's assessment using hair pull test, macroscopic global photography; dermoscopy and patient's assessment scale.

Patients were advised to wash their two days prior to the treatment. Hair Pull test was performed three times by the same clinician. A bundle of approximately 50-60 hair strands from the base close to the scalp, between the thumb, index finger and middle finger. The hair was firmly tugged away from the scalp, and the extracted hair was counted. Positive hair pull test was defined when more than 10% of hair was plucked. Standardised dermoscopic and macroscopic photographs were compared before and after the treatment. Vertex and oblique views of scalp were taken for macroscopic images. Dermoscopic photographs were taken at same areas before and after treatment.

At the end of 6 months, patients assessed their treatment outcomes on a scale of 0-3 (0: unsure; 1: Dissatisfied; 2: Satisfied; 3: Very satisfied). Patients feedback whether they would recommend this treatment to anyone else was also recorded as 'yes', 'no' and 'unsure'.

RESULTS

Hundred male patients in the age group of 20-50 were included in the study. According to Norwood-Hamilton scale, patients belonged to group II-IV of androgenetic alopecia. All the patients completed 3 sessions of PRP treatment at an interval of a month. Minor side effects like headache, redness and pain at injection site were

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noticed in few patients. There were no major side effects in any of the patients. There was no loss of patient at 6 months follow-up.

Physician's Assessment:

According to the physician's assessment which was done by comparing macroscopic global photographs and dermoscopy at baseline and at 6 months from the start of the treatment, an overall significant improvement in hair density per cm^2 area and thickness was seen at the sites of PRP injection. There was also an improvement in conversion of vellous hair into terminal hair (Figures 1-8).

Figure 1: Case 1 – Group A: (a) and (c) at baseline; (b) and (d) 6 months from the start of treatment

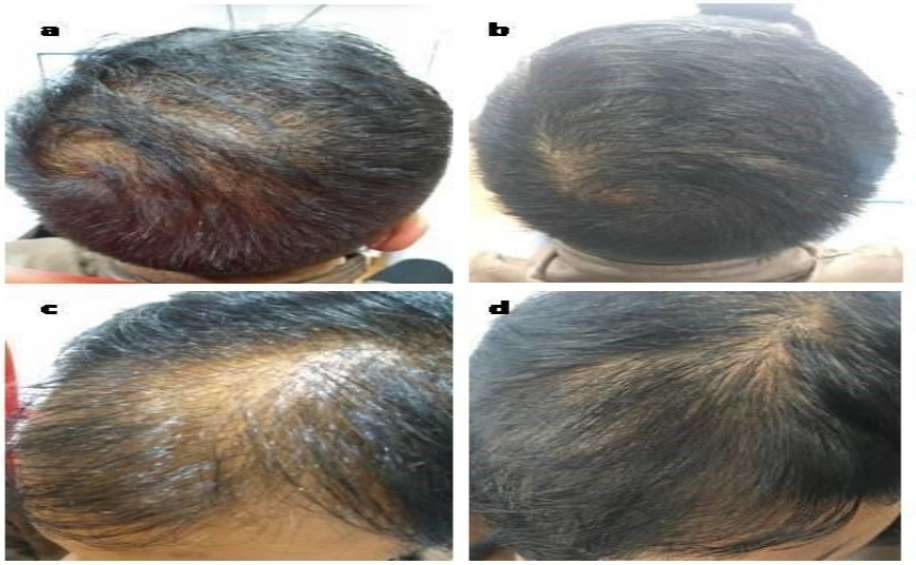

Figure 2: Case 1 – Group A: Dermoscopic photomicrographs 10 cm from glabella (a) at baseline; (b) 6 months from the start of treatment

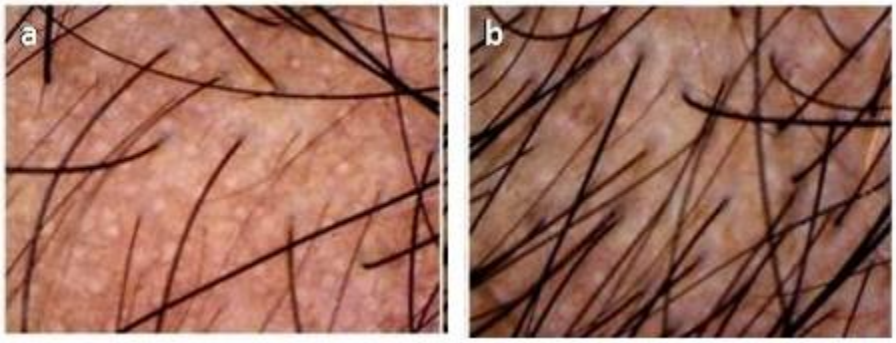

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Figure 3: Case 2 – Group A: (a) and (c) at baseline; (b) and (d) 6 months from the start of treatment

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Figure 4: Case 2 – Group A: Dermoscopic photomicrographs 15 cm from glabella (a) at baseline; (b) 6 months from the start of treatment

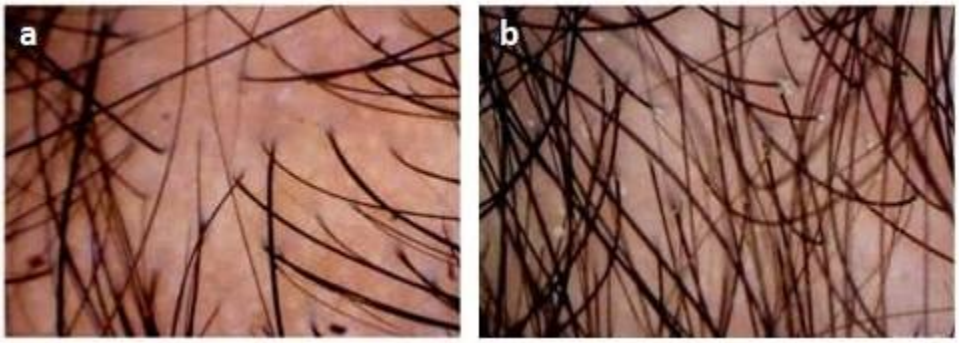

Figure 5: Case 3 – Group B: (a) and (c) at baseline; (b) and (d) 6 months from the start of treatment

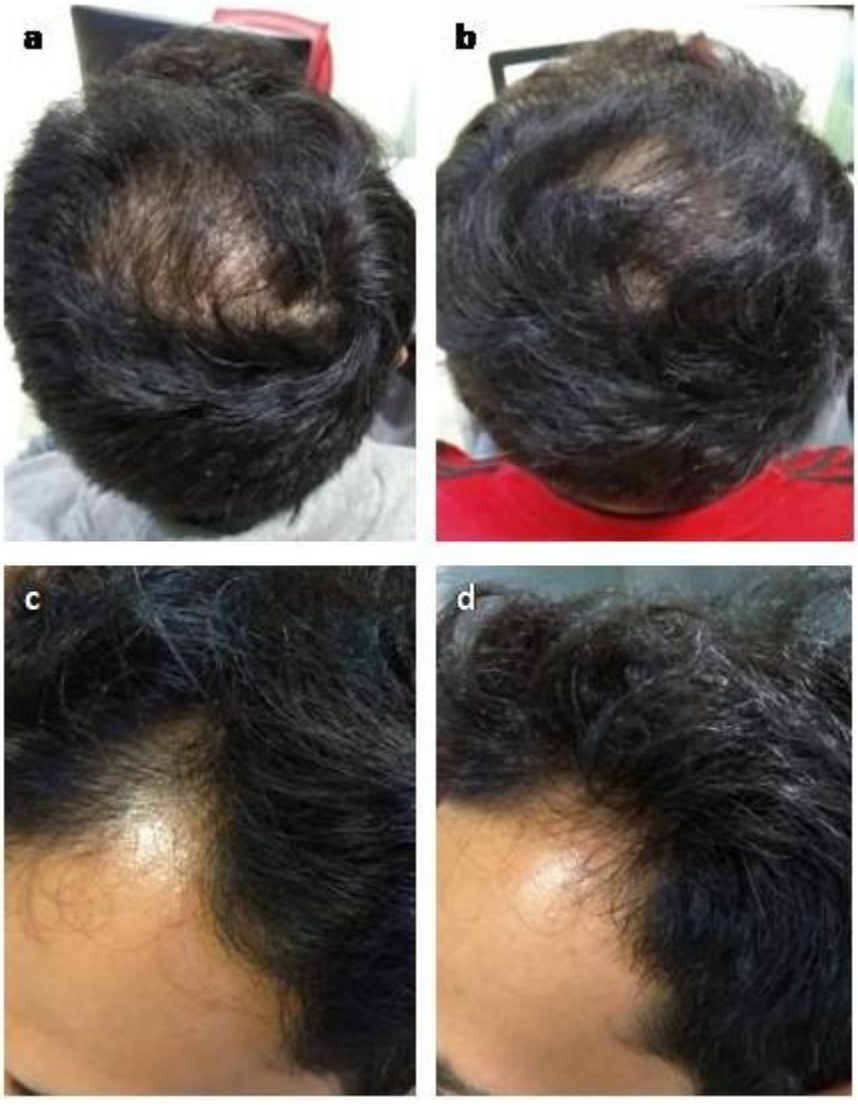

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Figure 6: Case 3 – Group B: Dermoscopic photomicrographs 20 cm from glabella (a) at baseline; (b) 6 months from the start of treatment

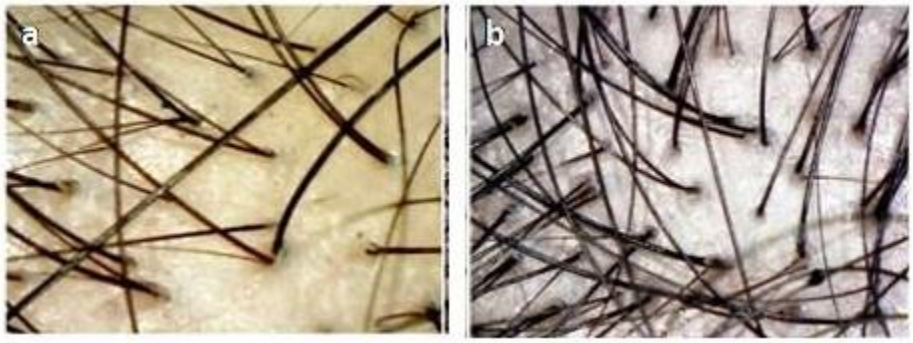

Figure 7: Case 4 – Group B: (a) and (c) at baseline; (b) and (d) 6 months from the start of treatment

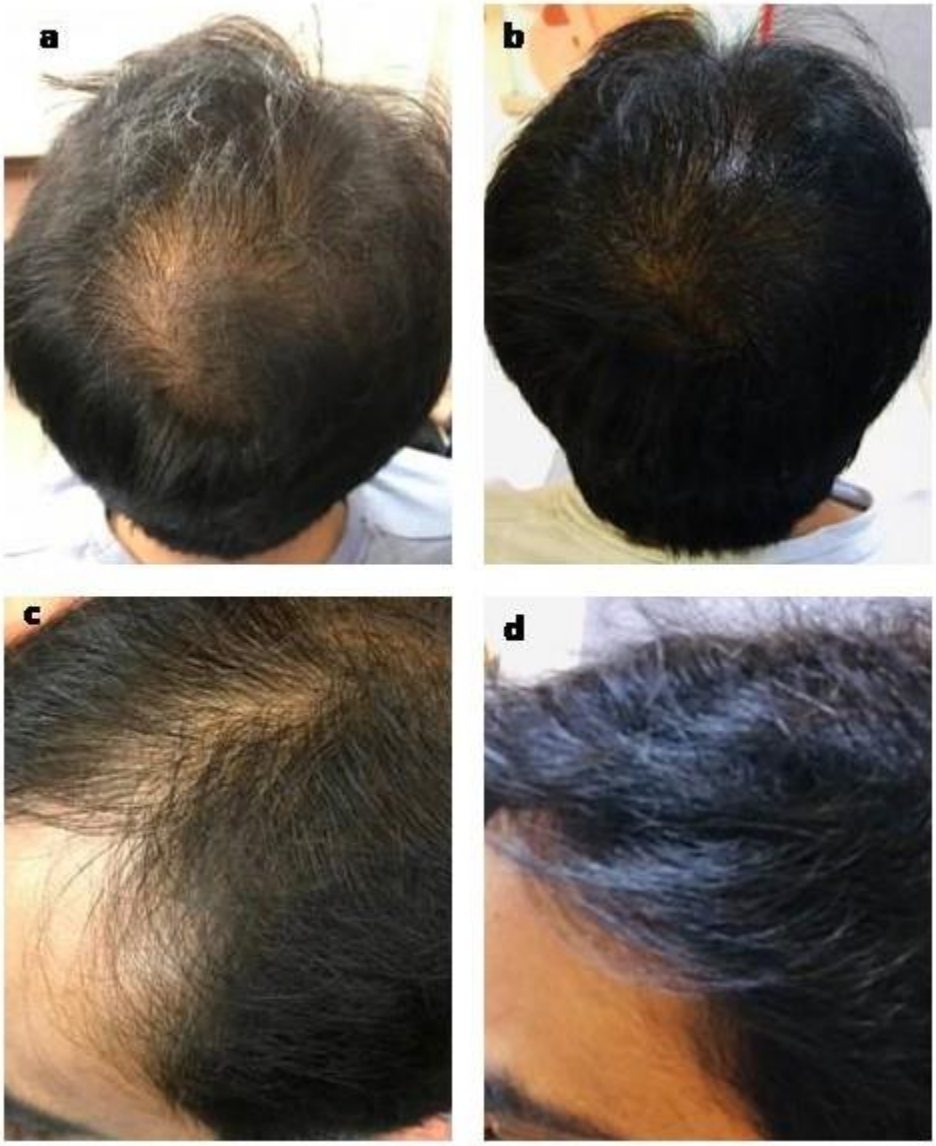

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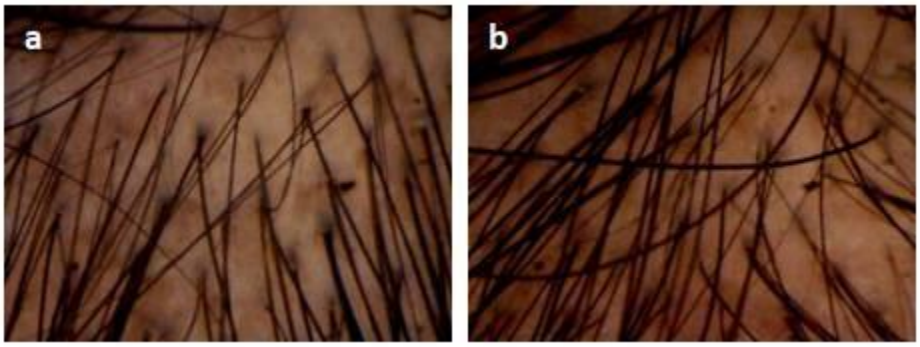
Figure 8: Case 4 – Group B: Dermoscopic photomicrographs 8 cm from left mid eyebrow (a) at baseline; (b) 6 months from the start of treatment



Before the start of treatment, all the patients (100%) had a positive hair pull test with a mean number of 10 hair. During the 6-month follow-up, the test was negative in the treated areas in 46 patients (92%) in Group A and 40 patients (80%) in Group B with average number of 3 hair.

Patient's Assessment:

In both the groups, there was a high overall patient satisfaction following treatment with 51% giving a score of 2 and 30% a score of 3. However, there was a higher percentage of satisfaction in group A compared to group B. Patients in group B on PRP with Non-minoxidil solution showed higher dissatisfaction compared to group A. 16% were dissatisfied and 14% were unsure of the treatment in group B (Table 2). One patient in group B was unsure of the treatment and was advised to undergo hair transplant.

Table 2: Patient Satisfaction Score

Group	Unsure (0)	Dissatisfied (1)	Satisfied (2)	Very satisfied (3)
Group A (n=50)	3	1	31	15
Group B (n=50)	7	8	20	15
Total	10	9	51	30

Out of 100 patients in the study, 77% said that they would like to recommend the treatment to someone else.

DISCUSSION

Male pattern hair loss is a cosmetic concern which causes psychological distress for patients and has an impact on quality of life. Patients seeking evaluation want successful treatments that aim at minimizing further hair loss as well as stimulating new hair growth.[10] PRP therapy is a minimally invasive, cost effective, biologically compatible procedure that has minimal or no side effects, thus making it more acceptable by the patients.[11] The current study was done to evaluate the efficacy of PRP for treatment for Androgenic Alopecia in male patients with topical application of Minoxidil and Non- minoxidil solutions. It also evaluated level of patient satisfaction after the treatment.

Even though PRP has been used for over a decade in patients with androgenetic alopecia, there is no single standard protocol regarding the preparation of PRP,

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number of sessions and interval between the two sessions.[12, 13] The rapid growth and interest in PRP therapy has also resulted in the development and commercialization of a variety of systems.[14] According to the guidelines by the manufacturer, we prepared Bio-PRP by a single centrifugation method and gave 3 sessions of PRP treatment at an interval of a month each. This was similar to Verma et al. and Cervelli et al. who gave PRP at monthly interval for 4 months and 3 months respectively.[13, 15] Injections can be done intradermally, subcutaneously, and interfollicular.[16] In our study, we administered Bio PRP at a depth of 1.5–2.5 mm intradermally which was similar to a study by Ince et al. in 2018.[16]

Due to the lack of a standardized protocol for preparation of PRP there is a variation in platelet activation, growth factor levels and platelet concentration because of which the results of the effect of PRP have been inconsistent. A pilot study by Kapoor and Shome suggested that intradermal injections of a formulation of multiple growth factors (QR 678) is safe and effective in treating both male and female pattern hair loss.[17] Borhan et al. prepared a non-activated PRP by mixing the platelet poor plasma with the PRP layer, and studied its effects. Their results showed slight improvement in hair density. The authors concluded that though positive clinical results were obtained, the use of non-activated PRP may have limited the production of growth factors, as compared to activated PRP.[18]

Since activation of platelets is believed to release growth factors, in our study, we prepared an autologous growth factor concentrate consisting of highly specific growth factors - platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF-1) and epidermal growth factor (EGF). These growth factors promote hair regrowth by binding to their respective receptors expressed by stem cells of the bulge region of hair follicles. They induce the proliferative phase of the hair follicle, prolong the anagen phase and promote angiogenesis.[4]

Hair pull test, global macrophotography and dermoscopy are subjective in nature making them difficult to validate and standardize owing to high variation among evaluators.[14] However, they have been used in several studies. According to multiple reviews, all studies reporting a pull test demonstrated reduction in hair loss 3 to 12 months following treatment with negative pull tests were defined as an average of 3 hair or less per pull.[19, 20] Global macrophotography using digital cameras has been commonly used in evaluating hair regrowth. It requires paired comparison of photographs taken in standardized patient positions from the baseline allows for assessing subjective outcomes following treatment.[14] Our study demonstrated improvement in hair quality and thickness loss when compared with baseline. However, various factors such as shooting angle, light, and usage of flash may show the hair density differently. [16]

Multiple randomized control trials have established the effectiveness of topical minoxidil therapy for the management of androgenic alopecia.[13] Minoxidil counteract the hair loss process by arresting follicular miniaturization and proloning the anagen phase. However, it may pose an increased risk of irritation to the skin, must be used indefinitely to prevent relapse and its effectiveness is limited by patient adherence.[11, 21]

When used together, PRP and minoxidil potentiate each other's action.[12] A study by AlvesR and GrimaltR in 2018 reported that the use of PRP in combination with the other treatment methods such as minoxidil or finasteride demonstrated a more pronounced clinical effect.[12] In our study, the result of the combined use of PRP and minoxidil/ non minoxidil solution was of particular interest. We found that the combined treatment resulted in a high patient satisfaction, lesser hairfall, improved density and volume. Our study also revealed that the positive results were greater in patients on minoxidil solution compared to non-minoxidil solution. Similar findings were reported by a study by Pakhomova et al. where the effects of complex therapy exceeded the effects of PRP monotherapy in terms of hair density; diameter of hair shafts.[12]

LIMITATIONS

The main drawback of our study was the use of a minoxidil/ non minoxidil solution along with PRP treatment. Due to lack of a control group, we were unable to assess the efficacy of PRP alone.

CONCLUSION

Autologous growth factor concentrate or PRP is an emerging treatment modality for patients with

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androgenic alopecia. When used along with a minoxidil or non-minoxidil solution, it results in increased hair volume, density, reduced hairfall and high patient satisfaction. However, further studies including controlled clinical trials with microscopic findings and longer follow-up are needed to confirm the efficacy of the treatment.

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