ORIGINAL ARTICLE

COMPARISON OF PLATELET RICH THERAPY ALONE WITH PLATELET RICH THERAPY ALONG WITH DAILY TOPICAL 5% PROCAPIL APPLICATION FOR THE TREATMENT OF ANDROGENETIC ALOPECIA

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Background: Androgenetic alopecia (AGA) affects up to 50% of males and 40% of females by the age of 50. It is the result of progressive, patterned hair loss that occurs in genetically predisposed individuals having hypersensitive androgen receptors in hair follicles. Due to the variable efficacy and adverse effect profile of FDA-approved drugs, newer and alternative modalities need to be utilized. As no prior study evaluated the efficacy of Procapil in combination with platelet-rich plasma (PRP), this study aimed to fill the research gap. The objectives were to assess the effectiveness of topical Procapil 5% combined with PRP vs PRP alone in androgenetic alopecia. **Methods**: It was a Quasi-experimental clinical trial conducted at the Tehsil Headquarters Hospital Takhtbhai Mardan. One hundred and sixty patients with AGA were selected and divided into two groups, 80 in each. Group A received 4 sessions of PRP alone, 4 weeks apart while Group B was treated with PRP in combination with topical 5%procapil solution applied twice a day. Final results are calculated at the end of 6 months using 7- 7-point patient' satisfaction and dermatologist evaluation scoring systems. **Results:** The mean age in Groups A and B was 29.34±5.3 & 30.22±4.8 respectively. Disease duration was comparable between both groups. At the final Assessment Greater proportion of patients in group B achieved better scores on Dermatologist evaluation and Patient satisfaction scales (p-value<0.05). **Conclusion:** It has been established that combining PRP with 5% Procapil yields better results in treating AGA compared to PRP used alone.

Keywords: Androgenetic Alopecia; Platelet-rich plasma; Procapil

Citation: Khoso H, Fahim M. Comparison of Platelet rich therapy alone with Platelet rich therapy along with daily topical 5% Procapil application for the treatment of androgenetic alopecia. J Ayub Med Coll Abbottabad 2024;36(2):299–304.

DOI: 10.55519/JAMC-02-12749

INTRODUCTION

The hallmark of Androgenic alopecia (AGA) is gradual non-scarring hair loss due to hair follicle miniaturization. Predominantly men are affected although females also suffer such type of hair loss.[1] Overall, its prevalence in men is 30-50% by age 50, varying among different ethnic groups. The highest prevalence of 80% is observed in Caucasians, while 58% of Asian men are affected.[2] The age of onset and progression of alopecia also varies among patients. In men, specific areas of the scalp include temporal and vertex areas, while the occipital region is usually spared.[3] Although multiple factors are involved in AGA pathogenesis, androgens play an important role in its pathophysiology. Dihydrotestosterone (DHT) is a metabolite of testosterone produced by 5-alpha-reductase and is the main pathogenic factor in AGA acting via Androgen Receptors (AR).[4] 5-alpha-reductase(type-2) is found in the outer root sheath of hair follicles and has got major role in AGA. Activation of AR affects expressions of various genes including those controlling hair growth cycle, leading to progressive miniaturization of hair follicles without affecting the stem cells.[5] In women, the comparatively low-level expression of alpha reductase enzyme results in less severe hair loss.[6]

Many treatment modalities have been tried in past to treat AGA. The two Food and Drug Administration (FDA) approved drugs are 5% topical minoxidil and 5-alpha-reductase inhibitors (finasteride). Minoxidil leads to vasodilation secondary to potassium channel opening and smooth muscle relaxation.[7] Previously its oral form was used to treat hypertension but due to multiple adverse effects and the availability of other safer antihypertensives, its use has diminished. When applied topically it increases the blood flow in the dermal papilla (DP), affects the expression of various genes involved in hair follicle growth and also downregulates the AR gene's function.[7] Its topical application may lead to acne, accelerated hair shedding, flushing, headache and dizziness/orthostatic hypotension.[8] Among the alpha-reductase inhibitors, Finasteride is a per os drug, selectively inhibiting type

II 5-alpha-reductase, that is predominantly expressed in hair follicles. Hair regrowth may be associated with certain none acceptable adverse effects like decreased libido, erectile dysfunction, gynecomastia and depression.[9] Looking at the adverse profile of FDA-approved drugs, other novel therapies need to be utilized.

PRP is a blood derivative previously used mainly for thrombocytopenia treatment.[10] Over time, due to better results its use was extended to other disciplines namely dermatology, obstetrics & gynecology, orthopedics, ophthalmology, and urology. Current dermatology applications include hair loss treatment, wound healing improvement, skin rejuvenation and scar appearance improvement.[11] To obtain PRP, 20cc whole blood is centrifuged along with an anticoagulant. There are multiple protocols for the centrifuge process, commonly soft spin followed by hard spine.[12] After centrifugation, a highly concentrated platelet mixture is obtained containing a variety of growth factors inside the Alpha granules such as platelet-derived growth factors (PDGF), vascular endothelial growth factor (VEGF), epithelial growth factor (EGF), transforming growth factor-beta (TGF beta), and insulin-like growth factor (IGF).[13] These growth factors are believed to enhance angiogenesis& neovascularization, cellular proliferation & differentiation, all processes mandatory for hair growth. IGF-1 has been shown to induce and prolong the anagen phase of the hair growth cycle.[14] Platelets also contain dense granules releasing numerous bioactive factors, importantly serotonin, histamine, dopamine, calcium, and adenosine, contributing to membrane permeability and inflammation modulation.[15] Studies suggest that PRP induce the proliferation of dermal papilla (DP) cells by activating extracellular Tyrosine kinase (ERK) and protein kinase B (Akt, an anti-apoptotic signalling molecule) signalling that results in the prolongation of the anagen phase and preventing apoptosis.[16]

A minimum of three PRP sessions are required to see encouraging hair regrowth in AGA.[17] The ideal interval between two sessions depends on the duration of growth factors release and the speed of hair growth. It has been found that upon activation, platelets continue to release growth factors for up to 10 days. Thus, the interval of either 2 weeks or 1 month may be chosen. However, because of the slow speed of hair growth (around 0.3 mm per day), it may be prudent to give monthly treatments and the beneficial effects are expected to continue for many months.[18]

Very little data is available on Procapil, its precise mechanism of action, and its efficacy in androgenetic alopecia. Very few studies evaluated its role in AGA and it is available in over-the-counter hair care products. Procapil is composed of three active plant-derived substances, all of which contribute to hair growth at different stages.[19] These include oleanolic acid, which inhibits type 1& 2 alpha reductase enzymes, resulting in decreased conversion of testosterone into DTH; apigenin, which is involved in vasodilation; and biotinyl-GHK, which contributes to enhanced anchoring of the hair with the strengthening of inner and outer root sheaths. Similarly, procapil is involved in regulating several genes affecting cellular metabolism, inflammation, antioxidant activities, matrix remodelling, and angiogenesis.[20]

MATERIAL AND METHODS

It was a prospective trial consisting of one hundred and sixty male patients, eighty in each group, keeping the power of the test at 90% and the confidence interval at 95%. After getting approval from the hospital administration, patients were divided into two groups using a non-probability consecutive sampling technique. Written consent was obtained from all patients along with an explanation of the study design, duration and possible adverse outcomes and complications.

PRP was prepared by collecting 20 ccs of fresh blood in sodium citrate-containing bottles under aseptic precaution. The protocol of soft spin (2000revolution/minute for 6 minutes) and hard spin (4000 revolutions/minute for 10 minutes) were applied. After collecting concentrated plasma, 1cc syringes were used to inject it intradermally. Group A received four sessions of PRP 4 weeks apart while group B received the same therapy in combination with 5% topical Procapil solution,5 puffs twice a day for 6 months. Basic demographic data like age, gender, and duration of disease were collected along with disease severity and pattern assessed by the modified Norwood-Hamilton score. The results were finalized after 6 months after the start of the first treatment session based on, Dermatologist evaluation, and patients' satisfaction scores, keeping a p-value of <0.05 as significant.

All male patients with hair loss (Hamilton score II -V), between the ages 18–50 years and willing to undergo the procedure were included in this study

Screening was done for Hepatitis B and C. All other conditions contributing to hair loss were excluded such as thyroid abnormalities, anaemia, connective tissue diseases malnutrition etc. Similarly, patients with Thrombocytopenia (low platelet count), hemodynamic instability (Hypotension, Cardiac failure) and other

conditions predisposing to excessive bleeding as well as local scalp infections and a history of allergy to previous sessions of PRP were also excluded.

Norwood-Hamilton classification[21]

1: There is either no recession or very little recession in the frontotemporal hairline region.

2: The hairline in the frontotemporal region shows a symmetrical, triangular recession. Even though the middle of the frontal region exhibits some hair thinning or loss, it is less pronounced than in the frontotemporal region.

3. Hair thinning becomes obvious. It becomes evident that there is a significant frontotemporal recession.

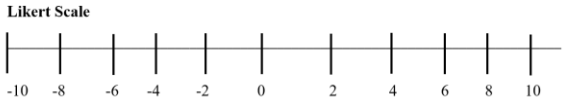
4: There is severe frontal and frontotemporal hair loss. The vertex has a noticeable thinning. There is a distinct band structure that separates these two zones.

5: In type 4, the hair band gets thinner. Vertex and frontotemporal regions show a greater percentage of hair-free areas.

6: Even in the band region, the hair loss is more obvious. Hair-free areas in the frontotemporal region converge with those in the vertex.

7. The is the most severe form. It extends rearward from the front of the ear. There is now only a horseshoe-shaped patch of hair covering the rear area.

Assessment Tools: One objective (Dermatologist evaluation score) and one subjective (Patient satisfaction score) assessment tool was utilized to evaluate hair regrowth. Hair regrowth was assessed by 2 dermatologists, filling the Proforma before and after the conclusion of the study. Each patient was evaluated based on 7- a point Likert scale. Excellent, Moderate and Slight hair regrowth categories consisted of those patients achieving some degree on improvement in hair growth. On the other side No change, Slight hair loss, Moderate hair loss and Extreme hair loss categories included groups of patients noticing no beneficial effects after 3 sessions of PRP. Similarly, Patient satisfaction with the treatment modalities was classified as very satisfactory, moderately satisfactory, slightly satisfactory, slightly unsatisfied, moderately unsatisfied, and very dissatisfied base on a 7-point patient self-evaluation questionnaire given to the patients to fill out according to their own perception of hair regrowth after 6 months.



Patient satisfaction score

Score	Level of satisfaction
0	No change felt
2–4	Slight satisfactory
6–8	Moderately satisfactory
10	Very satisfactory
-2 – -4	Slight dissatisfied
-6 – -8	Moderately dissatisfied
-10	Very dissatisfied

Dermatologist evaluation score

Score	Level of hair regrowth seen
0	No change seen
2-4	Slight hair regrowth was seen
6-8	Moderately hair regrowth is seen
10	Excellent hair regrowth is seen
-2 – -4	Slight hair loss
-6 – -8	Moderately hair loss
-10	Extreme hair loss

Data Analysis: Statistical software for social science (SPSS Version 24) was used to enter and analyse the data. The mean & SD were calculated for age, disease duration and age of onset. Both groups were compared by age, disease duration, the modified Norwood-Hamilton score, and responsiveness to understudy modalities in the form of patient satisfaction, and Dermatologist evaluation scores. A chi-square test was applied to compare the efficacy in both groups, using a two-sided $p<0.05$ as significant. Results are summarized in the form of Tables, Pie charts and column charts.

RESULTS

One hundred and sixty male patients with androgenetic alopecia were enrolled in this study,80 in each group. The basic demographic and clinical data of all patients are shown in Table-1. The mean age and disease duration were 29.34±5.3 & 3.9±1.3 years in Group A and 30.22± 4.8&4.03±1.8 years in Group B. Based on the Norwood-Hamilton scoring system, most of the patients in this study were in II-IV range.

More than 47% of patients had positive family history. After 6 months 25%,13.75% and 10% of patients in Group A were in the Slight, Moderate and very satisfactory range. On the other hand, in Group B the Slight, Moderate and very satisfactory categories consisted of 35% 23.75% and 13.75% patients (p-value=0.0022), Figure-2. Similarly, based on Dermatologist evaluation 11.25%,16.25% & 30% in Group A and 15%, 23,75% & 38.75% of patients in Group B were in the Excellent, Moderate and Slight Hair regrowth range respectively (p-value=0.0069), Figure-3. Overall improvement was seen mostly in patients with early forms of AGA (II-III).

Table-1: Basic demographic data

Parameter	Group A	Group B	*p*-value
Number of patients	80	80	
Age	29.34±5.3	30.22±4.8	0.27
Disease Duration	3.9±1.3	4.03±1.8	0.60
Family History of AGA	49.4%	47.8%	0.84
Norwood-Hamilton classification			
II	21	25	
III	23	20	
IV	20	18	
V	16	17	

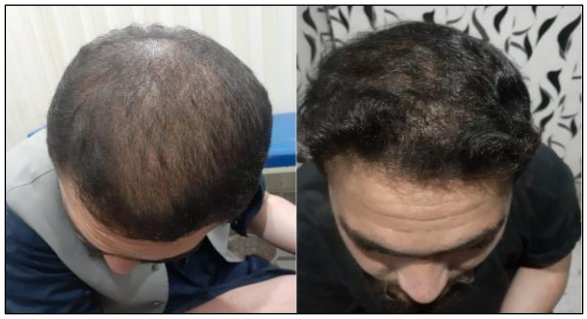


Figure-1: A & B. Before and after 3 sessions of PRP in combination with Procapil

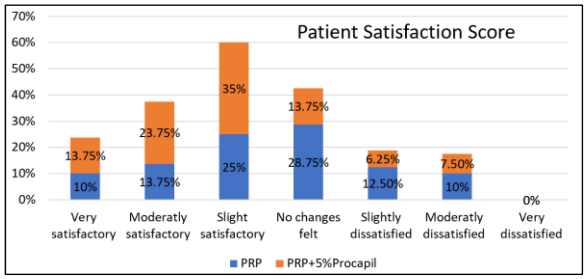


Figure-2: Patient satisfaction after 6 months

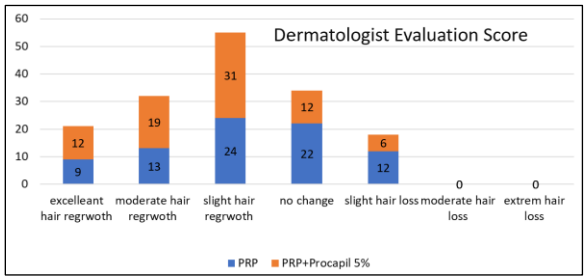


Figure-3: Hair regrowth based on 7- -point dermatologist evaluation scoring system

DISCUSSION

Androgenetic alopecia, commonly known as pattern baldness, is a prevalent form of hair loss affecting millions worldwide. This condition is characterized by a gradual thinning of hair, typically starting at the temples or crown of the head, in a predictable pattern influenced by genetics and hormones. Androgenetic alopecia is primarily driven by the hormone dihydrotestosterone (DHT), which shrinks hair follicles, shortening their growth phase and leading to progressively finer and shorter hair strands in genetically predisposed individuals.[22] Among many different treatment options available, Procapil is a newer drug with few studies conducted so far on its efficacy in AGA. This study aimed to evaluate the efficacy of this newer treatment modality with a favourable adverse effects profile.

In this study, 40 patients used Procapil solution in combination with PRP while another group consisting of the same number of patients received PRP-only therapy. At the end of 6 months, patients in the combination group achieved significant hair regrowth in terms of subjective (patients' satisfaction) and objective (Dermatologist evaluation) 7-point scoring systems, (*p*-value <0.05).

The efficacy of PRP in AGA was evaluated by Navakumar Manickam *et al* in a prospective trial consisting of 30 patients. The mean age, disease duration and number of patients based on the Norwood system was comparable to our study. Four sessions of PRP were done three weeks apart. At the end of 4th month, regardless of the area of involvement, more than 60% of patients have either mild, moderate or excellent improvement. Similar to our study better results are seen in patients with earlier stages of AGA.[23]

A Pakistani study conducted by Aftab Kanza et also assessed the efficacy of PRP by enrolling 19 female and 31 male patients having AGA. Most patients who had a disease duration of fewer than 2 years were administered in 3 sessions four weekly. Satisfactory response was defined by a patient 7-point satisfaction score and a negative hair pull test. Overall, 72% of patients had satisfactory responses, inversely correlated with advancing age and the presence of comorbidities.[24]

Kuldeep Verma *et al* compared PRP with 5% topical Minoxidil in the treatment of AGA. The mean age and number of patients in the Norwood grading system was comparable to our study Twenty patients used 5% Minoxidil solution twice a day and another group of twenty patients received 4 sessions of PRP one month apart. After 6 months overall there was no difference regarding the Hair Pull Test between the two groups but patient satisfaction score was significantly higher in patients receiving PRP (*p*-value=0.001). Importantly higher the platelets count, the better the results.[25]

A prospective interventional study consisting of 60 patients compared PRP with topical Minoxidil 5% and finasteride 0.1%. Patients were randomized into two groups. Group A was given PRP therapy at 0,1,2,3 and booster dose at 6 and 12 months while patients in Group B applied minoxidil fortified with

finasteride twice a day for 12 months.). Analysis was done with the help of global photography, a standardized hair growth questionnaire, and patient satisfaction score. After 12 months, compared to baseline hair regrowth was observed in the majority of patients but no statistical difference was seen between the two groups (*p*-value >0.05), showing that PRP is a cost-effective and safer therapy with good patient compliance.[26]

PRP in combination with 5% Minoxidil was compared with Minoxidil and PRP alone in a study conducted in Russia. The basic demographic profile was similar to our study. Patients received 4 sessions of PRP 1 month apart either alone (Group A-22 patients) in combination with 5% Minoxidil (Group B-25 patients), or Minoxidil 5% alone twice a day (Group C-22 patients). After 4 months, Patients in the combination group achieved better results in terms of hair density, hair shaft diameter, and decrease in vellus and telogen hairs (*p* value <0.05).[27]

An Indian study evaluated the effectiveness of PRP combined with Procapil (Group A) VS PRP combined with a cocktail containing Topical Redensyl, Saw Palmetto, and Biotin (Group B). Patients in both groups were treated with three sessions of PRP three weeks apart. After 6 weeks statistically significant results were observed in Group B in terms of reduction of AGA grading based on the Norwood-Hamilton classification (*p* value=<0.0001) and Global Photographic Assessment (*p* value=<0.0001).[28]

CONCLUSION

In this study, we compared the efficacy of PRP in combination with topical 5% Procapil in a prospective manner and it is concluded that combining Procapil solution with PRP gives better results than PRP alone in the treatment of Androgenetic Alopecia.

Limitations of the Study

With only 160 patients, the study's results may not be representative of the broader population, limiting the generalizability of findings. PRP contains numerous growth factors that help in hair regrowth, but it couldn't be ascertained that this improvement will be maintained without further PRP sessions as there was no long-term follow in our study. Importantly very few studies are available on the efficacy of Procapil in AA, so further large-center randomized studies are needed.

AUTHORS' CONTRIBUTION

HK: Data analysis, conceptualization, Critical review.
MF: Data collection, Critical review, Final approval

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Submitted: December 18, 2023	*Revised: February 6, 2024*	*Accepted: February 21, 2024*

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