The Effect of Platelet Rich Plasma on the Treatment of Androgenetic Alopecia Compared to Placebo

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Introduction:

Platelet-rich plasma (PRP) is an autologous preparation of platelets in concentrated plasma that contains a platelet concentration above basal concentration[1]. When the platelet-a granules become activated, numerous growth factors are released. The use of PRP in dermatology has shown to aid in tissue regeneration, fat grafting, skin rejuvenation, wound healing, and alopecia.[2]

Androgenetic alopecia (AGA) is commonly known as male pattern baldness[3]. Although named male pattern baldness, women are not excluded, affecting predominantly Caucasian women after menopause. The specific etiology of AGA is largely unknown with several genetic and environmental factors thought to contribute[5]. The hair loss is primarily observed bilaterally in the temporal area as well as the vertex in men, while it can also affect the anterior and mid-scalp.[4] In women, the hair loss tends to be diffuse thinning without a receding hairline.
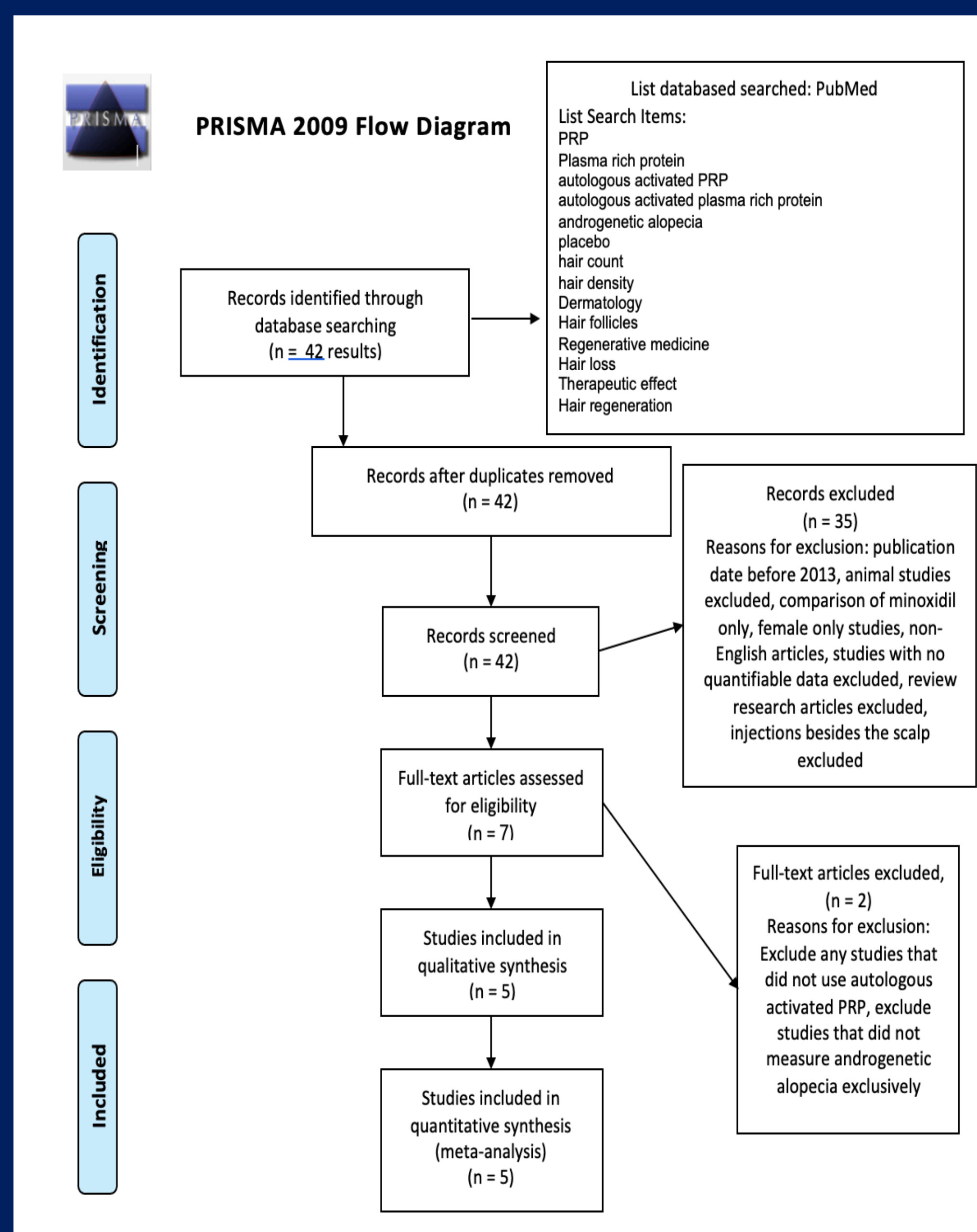
When treating androgenic alopecia, growth factors released from platelets may have an effect on stem cells in the bulge area of hair follicles by stimulating the development of new follicles and promoting neovascularization[6]. When the ectodermal stem cells, mesenchymal stem cells in the dermal papilla, and growth factors converge, the proliferative phase of hair growth is activated and prolonged, giving rise to a follicular unit[7].

Each growth factor has a role in the development and maintenance of new hair follicles. Platelet derived growth factor (PDGF) stimulates stem cell mitosis while transforming growth factor-b (TGF-b) activates the dermal papilla and inhibits apoptosis during the cell cycle[8]. Vascular endothelial growth factor (VEGF) helps by promoting microcirculation during the follicular growth process[9]. This poster will display the comprehensive analysis of research, investigating if PRP does in fact improve AGA outcomes.

Clinical Question:

In males and females, ages 18-60, with androgenetic alopecia, do platelet rich plasma injections more effectively treat hair growth (cosmetic and quantitative measures) compared to placebo?

Methods:

PRISMA 2009 Flow Diagram

List databased searched: PubMed

List Search Items:
PRP
Plasma rich protein
autologous activated PRP
autologous activated plasma rich protein
androgenetic alopecia
placebo
hair count
hair density
Dermatology
Hair follicles
Regenerative medicine
Hair loss
Therapeutic effect
Hair regeneration

Identification
Records identified through database searching (n = 42 results)

Screening
Records after duplicates removed (n = 35)

Records screened (n = 42)

Records excluded (n = 35)
Reasons for exclusion: publication date before 2013, animal studies excluded, comparison of minoxidil only, female only studies, non-English articles, studies with no quantifiable data excluded, review research articles excluded, injections besides the scalp excluded

Eligibility
Full-text articles assessed for eligibility (n = 7)

Full-text articles excluded, (n = 2)
Reasons for exclusion: Exclude any studies that did not use autologous activated PRP, exclude studies that did not measure androgenetic alopecia exclusively

Included
Studies included in qualitative synthesis (n = 5)

Studies included in quantitative synthesis (meta-analysis) (n = 5)

Results

Overview of Studies Reviewed

	Gentile et al[10]	Rodrigues et al[11]	Kachhawa et al[12]	Alves et al[13]	Paththinige et al[14]
Patient, N	23	26	44	22	28
Population	19-63 year old males with androgenetic alopecia (MPHL stages IIa-IV)	18-50 year old males with presentation of AGA III vertex profile according the Hamilton-Norwood scale.	18-55 year old males with diagnosis of androgenic alopecia with Hamilton-Norwood Grade III to VI	18-65 year old males and females/ Men selected had Hamilton-Norwood patterns II-V while women selected were Ludwig Stage I-III.	20-50 year old males and females with androgenetic alopecia
Gender	M: 100%	M: 100%	M: 100%	M: 50% F: 50%	M: 96.5% F: 3.5%
Duration of Study	injections every 30 days x 3 visits	20 injections (totaling 2 mL) every 15 days x 4 visits	A total of six treatments were performed every 21 days	Injections every 30 days x 3 visits	4 PRP treatments at baseline,3 weeks, 6 weeks, and at 14 weeks
Follow up	2 years	2 years	4.5 months	6 months	7 months
PRP Preparation	Casacade-Selphyl-Esforax system (single spin; 1100g for 10 min); Platelet Rich Lipotransfert system (single spin; 1200 rpm for 10 min); sodium citrate as anticoag	Amable et al method: autologous serum was prepared without anticoag, single spin (1258g for 15 min); 1 mL of serum was added to blood sample with citrate acid.	Double spin method of 1200 rpm for 8 minutes and again at 2400 rpm for 4 minutes	Single spin with addition of sodium citrate at 460g for 8 minutes	Double spin method utilizing the Dr. PRP Kit
Blinding Study	Evaluator blinded	Double blinded	Double blinded	Double blinded	Compares to baseline with no placebo
Groups	Half-head group study (PRP vs. placebo)	PRP (n=15) and control (n=11)	Half-head group study (PRP vs control)	Half-head group study (PRP vs control)	All patients treated with PRP
Endpoints (Measurements)	Hair count, hair density, terminal vs. vellus hair density	Hair count, hair density, anagen percentage, terminal-to-vellus ratio	Hair thickness and density along with a hair pull test and patient satisfaction scores	Global photography, hair count and density along with terminal hair density, anagen and telogen percentage and anagen to telogen ratio were analyzed.	Macroscopic Photography, hair count and hair density. Satisfaction questionnaires.

Figure 1: Patient receiving PRP injections into the scalp
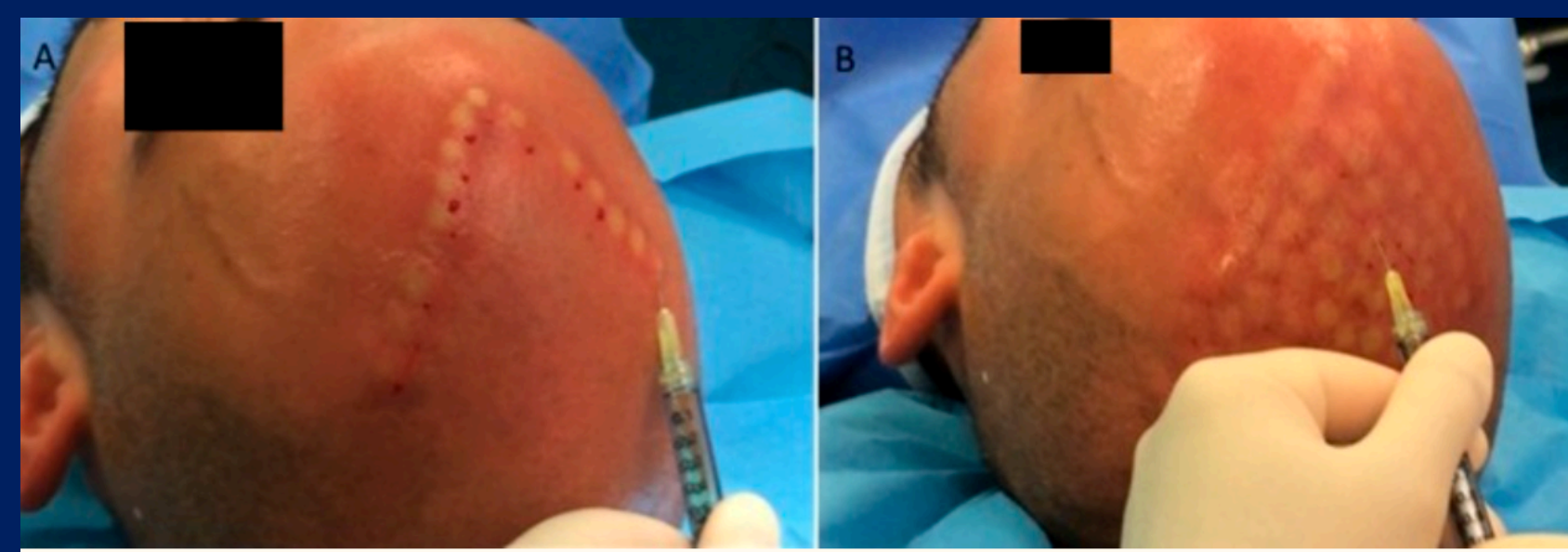
Gentile et al[10]:
Compared to baseline, the PRP group had a mean increase of 33.6 hairs vs the control which had a decrease of 3.2 hairs (P<0.0001). Improvement of hair density was statistically significant in the PRP group mean increase in total hair density of 45.9 hairs per cm² compared with baseline while there was a mean decrease of 3.8 hairs per cm² in the control group (P<0.0001). Terminal hair density showed significant improvement by 40.1 hairs per cm² in the PRP group compared to baseline while it decreased by 5.6 hairs per cm² in the control area (P= 0.0003). There were no statistically significant differences in vellus hair density between the study and the control area after 3 months.

Rodrigues et al[11]:
For hair count, the PRP group showed a significant increase in counts before application and 3 months after the last application (P=0.016) compared to the control group who showed a slightly, but not significant increase (P=0.320). Regarding hair density, the PRP group displayed a significant increase between the baseline and follow up values (P=0.012) compared to the control group where no difference was observed (P=0.206). Anagen percentages were significantly increased in the PRP group (P=0.007) compared to baseline. However, between the 15 days post injection measurement and 3 months post injection measurement, the increase was not maintained (P=0.703). With the control group, there was no significant increase during any of the evaluations. The terminal to vellus ratio showed no significant different in the PRP group or in the control group when comparing the ratios before and after treatment (P= 0.955 PRP, P= 0.206 control)

Kachhawa et al[12]:
The hair pull test resulted in an average of three hairs by the fourth visit compared to an average of eight hairs at baseline. Subjective photos throughout the study showed improvement in hair growth. Subjective questionnaires resulted in 70% reporting improvement in hair quality and thickness.

Alves et al[13]:
At the final follow up, of 6 months, the PRP treated area had a mean increase in total hair density of 12.8 ± 32.6 hairs/cm2 with a decrease on the control side. Improvement in mean total hair density with PRP was statistically significantly compared to the control with p <0.05 after both 3 and 6 months. There was no statistically significant increase in total hair count nor hair density between the PRP and placebo groups.

Paththinige et al[14]:
Compared to baseline the total hair density statistically increased each treatment with a p value of <0.001. Hair density measured at T6, which was 7 months post baseline, was 161.83 + 20.687 while baseline was 102.25 + 18.463. Macroscopic photos showed subjective improvement in hair growth.

Discussion:

All 5 studies that were reviewed demonstrated that PRP had a significant improvement in hair count, hair density, and overall hair growth in patients with androgenetic alopecia compared to the placebo.

Limitations
- Lack of standardized treatment protocol application of PRP in addition to standardized evaluation methods such as the addition of activators, the amount of time spent in the centrifuge and speed, platelet concentration, and the volume of blood used. Treatment protocols varied between the number of sessions, the time interval between treatments, duration of treatment, and the follow period.
- Relatively small sample size, making it difficult to assess for efficacy.
- With Paththinige et al, the study did not have a control group and only compared PRP's effectiveness to baseline measurements taken.
- Short duration of study and follow up after the treatment phase. Only Gentile et al reported relapse in 4 of their patients 16 months after treatment who were then retreated so it is unclear if other studies had relapses given the shorter follow up time frame.
- Subjective measurements like the hair pull test and patient satisfaction questionnaire

With the majority of the studies exclusively testing males, there could be some possible selection bias as androgenetic alopecia can also affect women as well. Also, with the subjective patient satisfaction questionnaires, the questions were not published, thus, making it difficult to assess for any bias. There was no evidence of publication bias or funding/sponsorship bias with any of the 5 studies reviewed.

All studies statistically compared each group's measurements with p-values, which emphasized that all results were statistically significant and not due to random chance. Of all the objective measurement findings, all measurements for the PRP groups were proven to be statistically significant with p-values<0.05, demonstrating PRP's effectiveness compared to placebo which showed many p-values >0.05.

Figure 2: Patient before and after treatment with PRP

Conclusion:

PRP effectively improves hair growth and density is those affected by AGA with limited adverse effects. PRP injections have proven to be safe with minimal invasiveness and no major adverse effects noted. Mild pain during injection was the most reported side effect and no infection or ecchymosis was reported. The downside of PRP injections is cost as Minoxidil and Finasteride continue to be the only FDA approved treatments for AGA. With PRP injections considered as off-label treatment for AGA, it's likely not to be covered by insurance. However, PRP is an appropriate alternative treatment with documented success in AGA.

Future Research:

In future studies, it would be beneficial to expand the research to compare PRP to the current standard treatments of AGA, including Minoxidil and Finasteride. It would also be helpful to create a standardized and qualitative measurement of results to allow for uniform comparisons across studies. Further exploration of PRP with the addition of growth factors in correlation to impaired hair growth may also be beneficial.

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