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Evaluation of the Hair Growth-Promoting Effects of Combined Treatment with Hair Growth Stimulants

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Abstract

The number of people with hair loss and thinning hair is increasing in Japan, regardless of age or sex, due to the aging of the population, advancement of women into the workforce, and increase in social stress. Hair loss and thinning have been attributed to genetic predisposition and hormonal imbalance; however, recent research has explored their relationship with environmental and psychological stress. Since 1981, we have been providing treatments focused on growing and nurturing hair in Japan, with the number of patients exceeding 2000 per year. We have conducted research on hair growth and regrowth for 40 years, focusing on factors such as hormonal imbalance, sebum, and stress, based on findings from our specialized manual treatments. In recent years, the number of patients taking finasteride has increased, and we have developed a treatment strategy to maximize its effectiveness. However, some patients either do not respond to the treatment or may not require the use of finasteride. In this study, we report on 1) cases in which efficacy was confirmed with manual treatment alone, 2) cases in which efficacy was confirmed with finasteride and manual treatment, 3) cases that did not respond to manual treatment and finasteride, and 4) cases with confirmed efficacy with continued treatment after discontinuation of finasteride.

Keywords

Hair Growth Products, AGA, Hair Growth

1. Introduction

In patients with androgenetic alopecia (AGA), the growth phase of the hair cycle shortens, while more hair follicles remain in the resting phase. This causes the

hair on the frontal and parietal areas to become soft, thin, and short, eventually resulting in forehead hairline recession and disappearance of the hair on the parietal area [1]-[8] (**Figure 1** and **Figure 2**). Dihydrotestosterone (DHT), a

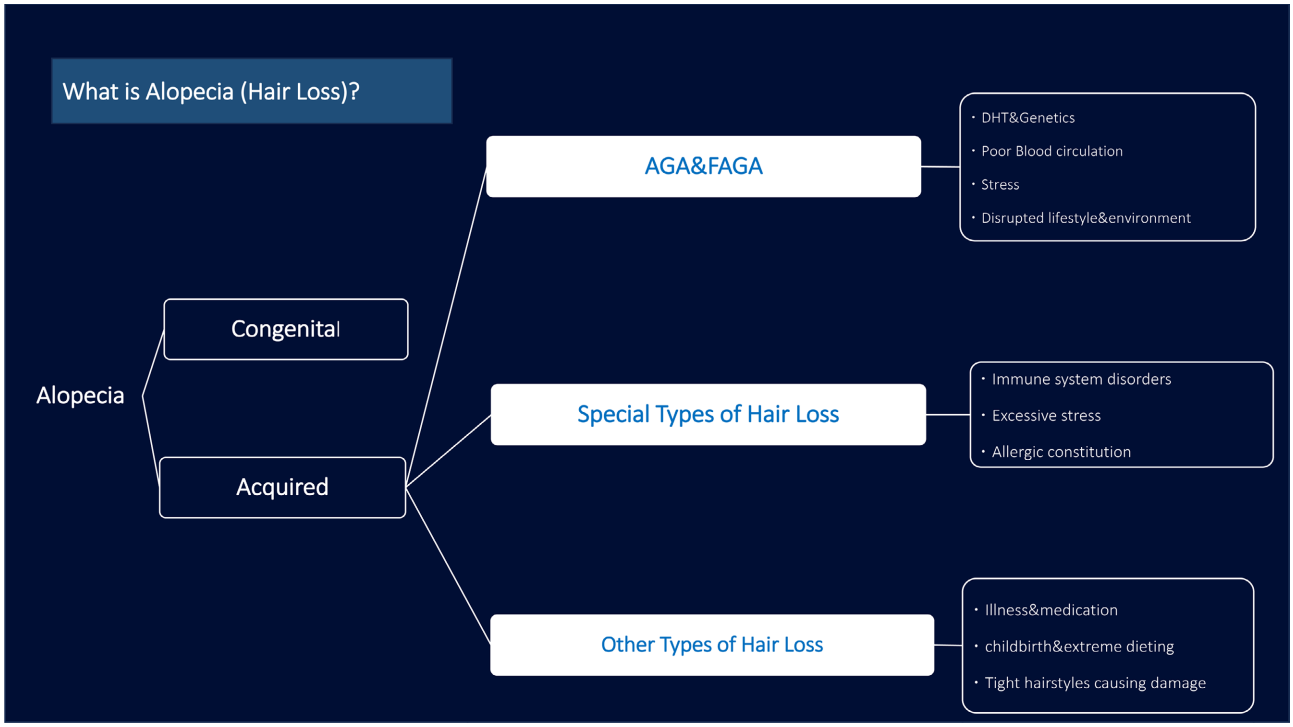


Figure 1. Classification of Alopecia.

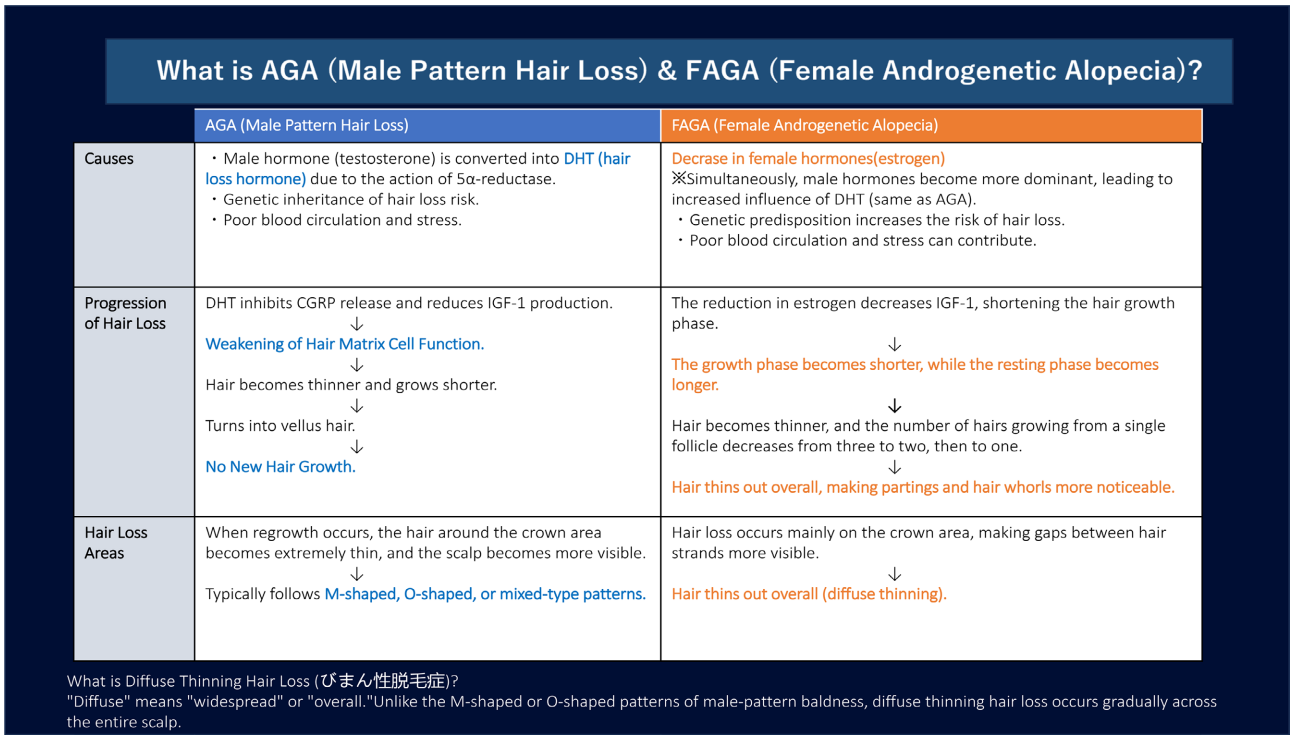


Figure 2. Causes and symptoms of AGA and FAGA.

converted form of the male hormone testosterone, and genetic predisposition are the main factors responsible for the development of AGA [9] [10]. Testosterone is important for bone and muscle development and for the maintenance of mental and physical health. It also makes body hair, such as beard and chest hair, thicker. Conversely, testosterone transforms male hormone-sensitive hair follicles of the frontal and parietal regions into fine soft hair [11]. Testosterone delivered to papilla cells in the frontal and parietal regions is converted to DHT by type II 5α-reductase, which binds to male hormone receptors and induces hair loss factors, such as transforming growth factor-β and Dickkopf-1, suppressing hair matrix cell proliferation and shortening the growth period [12].

The currently known genetic predispositions include a male hormone receptor gene polymorphism on the X chromosome and the presence of disease-related genes on autosomes [13]. A genome-wide association study has identified 624 SNPs associated with AGA [14]. Twin studies have estimated the heritability of AGA to be approximately 80% - 95% [15] [16]. Meanwhile, a study of monozygotic twins identified external and internal factors other than genetics and hormones, such as smoking, stress, ultraviolet light, and alcohol, to potentially be involved in alopecia [17].

Guidelines for the diagnosis and treatment of male-pattern and female-pattern hair loss, 2017 version (The Japanese Dermatological Association) recommend oral use of the 5α-reductase inhibitors finasteride and dutasteride, and topical use of minoxidil, which improves blood flow and cell growth, for the treatment of AGA (recommendation level A) [18]. Finasteride is an inhibitor of type II 5α-reductase that converts testosterone to DHT [19]. Dutasteride, like finasteride, is also an inhibitor of 5α-reductase; however, it acts not only on type II but also on type I, suppressing DHT production [20]. Although the mechanism of action of minoxidil has not yet been fully elucidated, studies have suggested that it activates SUR2B and opens KATP channels, which may promote cell proliferation, inhibit apoptosis of epithelial hair tissue cells (hair matrix cells), and improve blood flow in hair tissue, thereby promoting the transition from the resting to the growth phase and improving dwarf follicles by extending the growth phase [21].

Sebum secretion has also been found to be largely attributable to AGA [22]. The number of sebaceous glands is generally approximately 50/cm^2 in the extremities, 400 - 900/cm^2 in seborrheic areas, and 900/cm^2 in the scalp, indicating that the scalp has high sebum production [23] [24]. Sebum secreted from the scalp is a complex mixture composed of triglycerides, squalene, cholesterol esters, wax esters, and cholesterol [25]. Sebum secretion begins to increase at puberty, peaks at age 15 - 35, and decreases thereafter [26]. Throughout the active period of sebum secretion, the secretion is higher in men than in women, and the rate is maintained longer in men through their 50 s and 60 s, than in women, where it declines rapidly after menopause [27]. Patients with AGA produce more sebum than patients without AGA, and testosterone, one of the causes of AGA, increases sebum secretion [28] [29]. The amount of fatty acids in blacks and Caucasians has also been

reported [30]. Excess sebum becomes oxidized when exposed to air and blocks pores, causing inflammation within the pores, thereby inhibiting hair growth. Therefore, keeping the scalp clean is important to maximize the effectiveness of hair care by removing sebum from pores while maintaining adequate sebum.
Suppressing DHT and removing excess sebum promotes the production of insulin-like growth factor 1 (IGF-1) and improves the fundamental functions related to hair growth, thus increasing the effectiveness and efficiency of hair growth products [31].

Sensory nerves, which transmit pain, heat, and other stimuli to the brain, sense the stimulus information and release a substance called calcitonin gene-related peptide (CGRP). When the papilla cells receive CGRP, they release IGF-1, which activates hair matrix cells, and hair growth is promoted through division and proliferation [32] (**Figure 3**).

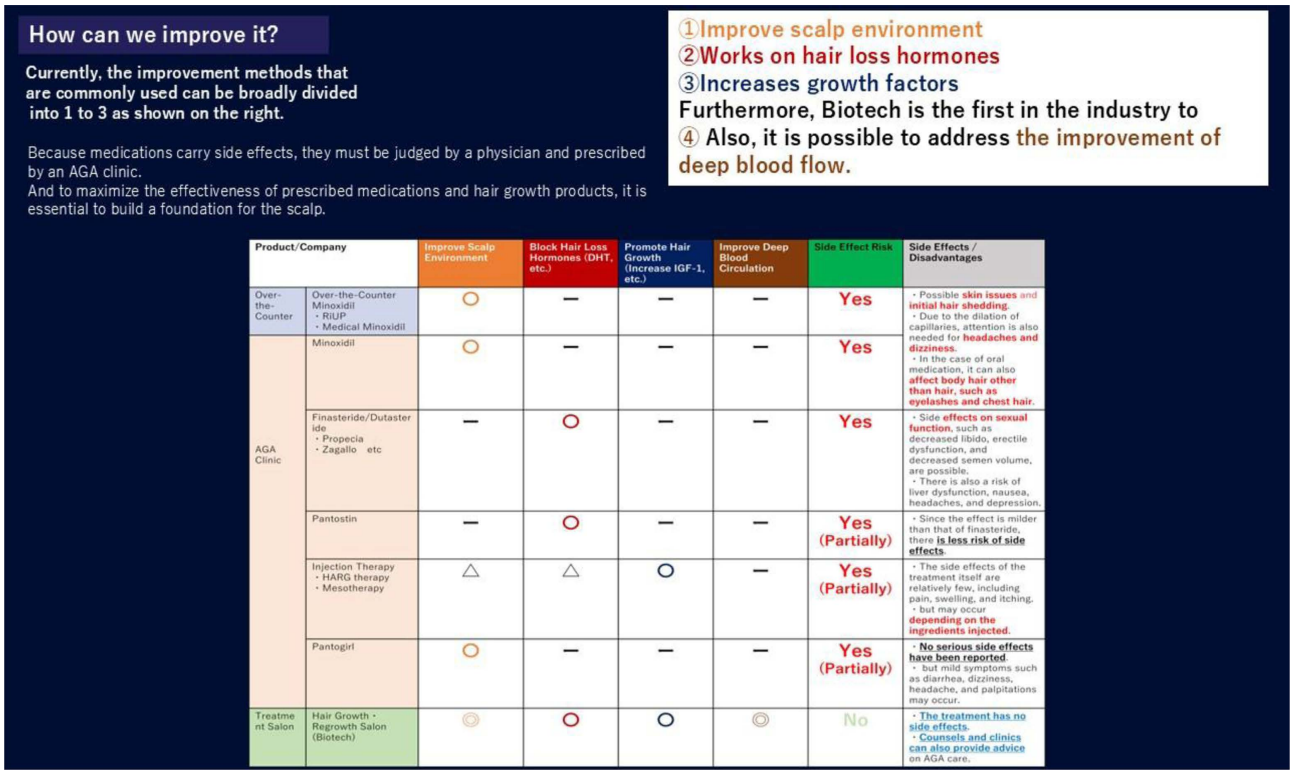


Figure 3. Approach to AGA and FAGA.

In this study, we focus on these three effects and report the clinical outcomes using our original treatment technology.

2. Methods

2.1. Eligible Examinees and Inclusion and Exclusion Criteria

Individuals who met all of the following inclusion criteria and did not meet any of the exclusion criteria were included in the study.

[Inclusion criteria]

1) Otherwise healthy Japanese men with thinning hair (AGA).

2) Japanese men in their 20 s to 50 s with AGA.

3) Persons who were able to give voluntary consent.

In this study, we aimed to recruit at least three participants with prior experience of medication use and three without such experience. Recruitment was conducted within the clinic by requesting cooperation from eligible patients. Among the participants who agreed to join the study, one individual had prior experience with medication but had already discontinued its use at the time of participation. This case is also reported in the study.

[Exclusion criteria]

1) Persons with skin diseases on the head other than AGA, such as wounds, eczema, or inflammation (redness).

2) Persons with skin diseases with desquamation (including fluke) such as atopic dermatitis on the head.

3) Persons with skin diseases such as acne or atopic dermatitis on the cheek area.

4) Any other person whom the practitioner deems inappropriate for this examination.

2.2. Restrictions

Regular medications should be discontinued unless deemed absolutely necessary.

2.3. Consent of the Examinee

At the study site (Biotech, Japan), before the start of the study, the study personnel fully explained to the subjects that their participation in the study was voluntary and that they would not be disadvantaged if they did not participate in the study. The subjects provided written consent to participate in the study. The study protocol was reviewed and approved by the Ethical Review Committee of Biotech (approval number: 001).

2.4. Treatment

Table 1 summarizes the treatment each subject received.

Images of the equipment and agents used in the treatment are summarized in Table 2 and Table 3.

The *α*, *γ*, and polization procedures are summarized in Figures 4-6. Each treatment session lasted between 90 to 120 minutes. Including counseling and other procedures, the total time spent in the clinic exceeded two hours per visit.

2.5. Imaging

Photographs were taken three times (before the procedure, after the third month from the start of the procedure, and at completion of the procedure) using a camera (OptioWG-2, Ricoh Co., Ltd.). Five locations were photographed: the AO, O, A, and left and right H sections. Photographs were taken while the hair was wet after rinsing.

Table 1. Subject information and treatment details.

Test Subject No.	Age	Gender	Surgery Start Date	Surgery Completion Date	Number of surgery	Surgery details	Taking medication	Medication start date	Devices used	Topical solutions used
No.1	27	men	May 2022	February 2024	1.5	Poration, α	Dutasteride	October 2022	Pollation InoExcel	Premium Scalp Lotion β
No.2	31	men	April 2018	January 2023	0.7	γ, α, Poration	Finasteride, Minoxidil	June 2018	Hair Esthetics Pollation InoExcel	Original Supplement, Premium Scalp Shampoo, Premium Beta
No.3	57	men	June 2021	February 2023	1.9	γ, α, Poration	Finasteride, Minoxidil	August 2021	Hair Esthetics Pollation InoExcel	Premium Scalp Shampoo, Premium Beta
No.4	37	men	October 2016	July 2024	1.6	Kneading Option + α, Cleansing & Shampoo Option + Poration	Finasteride, Minoxidil	February 2017		Premium Scalp Shampoo, Power Scalp Theraputa Premium Scalp Lotion β, Plus Scalp Essence Botanical Scalp Lotion, Premium Scalp Axel Essence, Plus β Glucan Plus Next Supplement
No.5	33	men	August 2020	September 2023	2	γ, α, and Poration	Finasteride, Minoxidil	October 2020	Hair Esthetics Pollation InoExcel	Original Supplement, Premium Scalp Shampoo, Beta, Step Supplement, Serum, Ong, R, Tilet
No.6	34	men	August 2020	May 2024	1.1	γ, α	Finasteride, Minoxidil	August 2018	Hair Esthetics InoExcel	Original Supplement, Premium Scalp Shampoo, Beta, Step, Supplement, Serum, Tilet
No.7	41	men	August 2023	January 2024	1.6	γ, α	No medication taken		Hair Esthetics InoExcel	Premium Scalp Shampoo, Premium Treatment, Premium Scalp Lotion β (Single Item), Botanical Scalp Lotion (Single Item), Premium Polish Mist Serum, Plus Step Supplement, Premium Select Supplement, Plus Scalp Cleansing, TILLET SMART-GEAR
No.8	59	men	October	June	1	γ, α	No		Hair	Premium Shampoo,

			2023	2024			medication taken	Esthetics InoExcel	Premium Scalp Lotion Beta, Brush H
No.9	30	men	March 2020	June 2024	2.1	*γ*, *α*	No medication taken	Hair Esthetics InoExcel	Premium Scalp Shampoo, Premium Scalp Lotion Beta (Single Item), Botanical Scalp Lotion (Single Item), Premium Poration Mist Serum, Plus Scalp Cleansing, TILLET SMART-GEAR
No.10	32	men	December 2022	June 2024	1.7	*A* with Kneading Option	No medication taken	Hair Esthetics InoExcel	Beta, Plus Essence, TILLET, Serum, Select, Step, Accel Essence, Next, Cleansing, : Avion Shampoo, Avion Treatment
No.11	39	men	April 2021	June 2024	2.1	*γ*, *α*, Poration	No medication taken	Hair Esthetics Pollation InoExcel	Beta, AccelEssence, StepSupplement, Select Supplement, Original Supplement, Beta-Glucan

Table 2. List of used products.

Product Name	Product Image	Full Ingredients
Premium Scalp Lotion *β* (Single Item) [Hair Growth Tonic]		Active Ingredients: Hinokitiol, Ethinylestradiol Other Ingredients: Loquat Leaf Extract, Seaweed Extract-1, Glycyrrhizin Acid 2K, DL-PCA Na Solution, Betaine, Sorbitol Solution, Glycine, Alanine, Proline, Serine, Threonine, Arginine, Lysine Solution, L-Glutamic Acid, POE Hardened Castor Oil, Dimethicone, Panthenyl Ethyl Ether, Squalane, Sodium Polyphosphate, POE (20) POP (4) Cetyl Ether, Trehalose, Triethylhexanoin, Tetraethylhexanoate Pentaerythritol, Nicotinic Acid Benzyl Ester, Menthol, Stearoylglutamic Acid 2Na, Natural Vitamin E, Tocopheryl Acetate, Concentrated Glycerin, BG, Ethanol, EDTA-2Na, Phenoxyethanol, Methylparaben, Propylparaben, Fragrance, and one additional ingredient.
Premium Scalp Shampoo		Water, Lauramidopropyl Betaine, Ethanol, BG, PEG-20 Sorbitan Cocoate, Cocoyl Methyl Taurine Na, Lauroyl Aspartic Acid Na, Triisostearic Acid PEG-120 Methyl Glucose, Betaine, Polyquaternium-10, Menthol, Scutellaria Root Extract, Senburi Extract, Cladosiphon Novae-Caledoniae Polysaccharide, Loquat Leaf Extract, Soybean Seed Extract, Aloe Vera Leaf Extract, Hydrolyzed Silk, Green Tea Leaf Extract, Isostearyl Hydrolyzed Silk AMP, Glycyrrhizin Acid 2K, Trehalose, Polyquaternium-64, o-Cymen-5-ol, Glucosyl Hesperidin, Panthenol, Pyrrolidinyldiaminopyrimidine Oxide, Polyquaternium-51, Pentylene Glycol, Citric Acid, Phenoxyethanol, Ethylparaben, Propylparaben, Butylparaben, Methylparaben, Fragrance.

Premium Treatment		Water, Cetearyl Alcohol, Glycerin, Isononyl Isononanoate, BG, Betaine, Alkyl (C12, 14) Oxyhydroxypropyl Arginine HCl, Hexa(Hydroxystearic Acid/Stearic Acid/Rosin Acid) Dipentaerythrityl, Ethanol, Olive Fruit Oil, Polyquaternium-48, Diethyl Sebacate, Arginine, Macadamia Seed Oil, Isostearyl Hydrolyzed Silk AMP, Tosylvaline Na, (Dihydroxymethylsiloxy) Hydroxypropyl Hydrolyzed Silk, Hydrolyzed Keratin (Wool), Creatine, Panthenyl Ethyl, Lauroyl Glutamic Acid Di(Phytosterol/Octyldodecyl), Tri(Caprylic/Capric Acid) Glyceride, Polysorbate 80, γ-Dodecalactone, Laminaria Ochroleuca Extract, Polyquaternium-51, Green Tea Leaf Extract, Pentylene Glycol, Peppermint Leaf Extract, Lecithin Hydroxide, Cladosiphon Novae-Caledoniae Polysaccharide, Sodium Hyaluronate, Hydroxypropyltrimonium Hyaluronate, Loquat Leaf Extract, Hydrolyzed Collagen, Soybean Seed Extract, Burdock Root Extract, Scots Pine Cone Extract, European Ivy Leaf/Stem Extract, Garlic Root Extract, Rosemary Leaf Extract, Roman Chamomile Flower Extract, Arnica Flower Extract, Lamium Flower/Leaf/Stem Extract, Watercress Leaf/Stem Extract, Citric Acid, Phenoxyethanol, Methylparaben, Propylparaben, Fragrance.
Premium Original Supplement		Pea Sprout Extract Powder (Pea Sprout Extract, Isomalt) (Swiss Manufactured), Indigestible Dextrin, Corn Germ Extract, Yeast (Contains Biotin), Zinc-Containing Yeast, Saw Palmetto Seed Extract Powder (Saw Palmetto Extract, Dextrin), Edible Refined Processed Fats and Oils, Plant-Derived Mineral Powder, Hydrolyzed Keratin (Hydrolyzed Keratin, Dextrin), Chlorella Powder, Feverfew Extract Powder, Millet Seed Extract, HPMC, Vitamin C, Cyclodextrin, Niacin, Calcium Stearate, Silica (Fine Particles), Calcium Pantothenate, L-Cystine, L-Threonine, L-Arginine, L-Methionine, Caramel Color, β-Carotene, Vitamin B6, Vitamin B2, Vitamin B1, Folic Acid, Vitamin B12 (Contains Gelatin in some products).
Premium Select Supplement		Olive Oil (Spanish Manufactured), Soybean Germ Extract, Garlic Extract Powder, GABA, Wasabi Extract, Ginger Extract Powder, Mozuku Extract, Grape Seed Extract, Cocoa Extract Powder, Raw Coffee Bean Extract Powder, Red Wine Extract Powder, Dried Royal Jelly, Swiftlet Nest, *Haematococcus Pluvialis* Extract, Gelatin, Glycerin, Glycerin Fatty Acid Esters, Beeswax, Cocoa Color, Antioxidant (γ-Oryzanol), Spice Extract, Vitamin A, Fragrance, Vitamin D.
Premium Scalp Accel Essence		Water, Ethanol, BG, Burdock Root Extract, Hawthorn Extract, Acetyl Tetrapeptide-3, Red Clover Flower Extract, Dextrin, Sodium Hyaluronate, PEG/PPG/Polybutylene Glycol-8/5/3 Glycerin, PEG-100 Hydrogenated Castor Oil, EDTA-2Na, Menthol, Citric Acid, Sodium Citrate, Methylparaben.

Premium Poration Mist Serum		Water, Ethanol, BG, Glycerin, Trehalose, Menthol, Glycyrrhizin Acid 2K, Loquat Leaf Extract, Mitsuishi Kombu Extract or Brown Algae Extract, Betaine, PCA-Na, Sorbitol, Serine, Glycine, Glutamic Acid, Alanine, Arginine, Lysine, Threonine, Proline, Dimethicone, Squalane, Tocopherol, Tocopheryl Acetate, Magnesium Ascorbyl Phosphate, Octapeptide-2, Nicotinic Acid Benzyl Ester, Panthenyl Ethyl, Tetraethylhexanoate Pentaerythritol, PPG-4 Cetes-20, PEG-50 Hydrogenated Castor Oil, Sodium Tripolyphosphate, EDTA-2Na, Phenoxyethanol, Propylparaben, Methylparaben, Fragrance.
Botanical Scalp Lotion (Single Item) [Hair Growth Tonic]		Active Ingredients: Tocopheryl Acetate, Glycyrrhizin Acid 2K, Hinokitiol Other Ingredients: BG, Ginger Extract, Hydrolyzed Soy Protein, Sodium Hyaluronate-2, Photosensitive Dye 301, Ginseng Extract, Angelica Extract-1, Aloe Extract-2, Rehmannia Extract, Heliotropium Extract, Ivy Extract, Velvetleaf Extract, Thyme Extract-2, Perilla Extract, Lauroyl Glutamic Acid Di(Phytosterol/Octyldodecyl), Menthol, Safflower Yellow, Rice Germ Oil, Squalane, Betaine, Concentrated Glycerin, Dimethicone, Persimmon Tannin, Trehalose, Sodium Carbonate, Dicaprylate Neopentyl Glycol, POE Hardened Castor Oil, POE (20) POP (4) Cetyl Ether, EDTA-2Na, Parabens, Fragrance, and One Additional Ingredient.
Plus Scalp Essence (Single Item)		Water, BG, Ethanol, Glycerin, Pea Sprout Extract, Pyrrolidinyldiaminopyrimidine Oxide, Capsicum Fruit Extract, Saccharomyces/(Black Sugar/Placenta Extract) Fermentation Liquid, Siberian Larch Wood Extract, Human Oligopeptide-1, Acetylneuraminic Acid, Oryzanol, Cladosiphon Novae-Caledoniae Polysaccharide, Geraniol, Glycosyl Trehalose, Hydrolyzed Hydrogenated Starch, PEG-60 Hydrogenated Castor Oil, Dimethicone, PPG-4 Cetes-20, Squalane, Dilaureoyl Glutamic Acid Lysine Na, Tocopherol, Arginine, Citric Acid, Sodium Citrate, Pentetate Sodium, Pentylene Glycol, Methylparaben, Propylparaben, Phenoxyethanol, Sodium Benzoate.
Plus Scalp Cleansing		Water, DPG, palm oil fatty acid PEG-7 glycerol, pentylene glycol, PEG-40 hydrogenated castor oil, diethyl succinate, allantoin, chili extract, Enantia chlorantha bark extract, oleanolic acid, burdock root extract, European black pine cone extract, ivy leaf/stem extract, garlic root extract, rosemary leaf extract, Roman chamomile flower extract, arnica flower extract, motherwort flower/leaf/stem extract, watercress leaf/stem extract, hydroxyl lecithin, glycerin, polysorbate 80, BG, ethanol, (acrylate/acrylic acid alkyl (C10-30)) crosspolymer, carbomer, potassium hydroxide, pentetic acid 5Na, fragrance or vanillyl butyl.
Plus Beta-Glucan		Black Yeast (Aureobasidium) Fermentation Liquid, Galacto-Oligosaccharide Syrup, Reduced Maltose, Polyamine-Containing Rice Germ Extract, Lactic Acid Bacteria (Sterilized), Dextrin, Starch Hydrolysate/Citric Acid, Fragrance, Vitamin C.

Plus Next Supplement		Reduced Maltose Syrup, α-GPC (Glycerophosphocholine), Erythritol, Processed Fats, Raspberry Fruit Powder, Lingonberry Extract Powder, Starch, Cellulose, Sugar-Transformed Hesperidin, Sweeteners, Acidulants, Baking Soda, Calcium Stearate, Micronized Silica, Fragrance, Thickeners.
Plus Step Supplement		Larch Cambium and Xylem Extract (Made in Russia), Cellulose, Vitamin C, Hesperidin, Calcium Stearate, CMC (Carboxymethylcellulose), Silica.
Plus Ong Water R		Water
Plus Ong Water R		Water
AVION. Shampoo CITRUS MUSK		Water, Lauramidopropyl Betaine, Ethanol, Cocamid DEA, Pentylene Glycol, Cocoyl Methyl Taurine Na, PEG-2 Caprylylamine, Lauroyl Asparagine Na, Triisostearic Acid PEG-120 Methylglucose, Betaine, Polyquaternium-10, Isostearoyl Hydrolyzed Silk AMP, Glycyrrhizic Acid 2K, Trehalose, Hibiscus Flower Extract, PCA-Na, Sodium Lactate, Arginine, Aspartic Acid, PCA, Glycine, Alanine, Serine, Valine, Isoleucine, Threonine, Proline, Histidine, Phenylalanine, PEG-40 Hydrogenated Castor Oil, BG, Citric Acid, Phenoxyethanol, Fragrance.

AVION. Treatment CITRUS MUSK		水 Sorbitol, DPG (Dipropylene Glycol), PPG-3 Caprylyl Ether, Ethylhexyl Palmitate, Behenyl Alcohol, Stearyl Alcohol, Behentrimonium Chloride, Isopropanol, Sebacic Acid Diethyl Ester, Ethanol, Polyquaternium-11, Lauroyl Arginine, Polyquaternium-7, Isostearoyl Hydrolyzed Silk AMP, Hydrolyzed Keratin (Wool), Hydrolyzed Sesame Protein PG Propyl Methylsilane Diol, γ-Dodecalactone, BG, PCA-Na, Sodium Lactate, Arginine, Aspartic Acid, PCA, Glycine, Alanine, Serine, Valine, Isoleucine, Threonine, Proline, Histidine, Phenylalanine, Hibiscus Flower Extract, Phenoxyethanol, Fragrance.
Finasteride Tablets		

Table 3. List of equipment used.

a. InoExcel

b. Hair Esthe

c. Poration

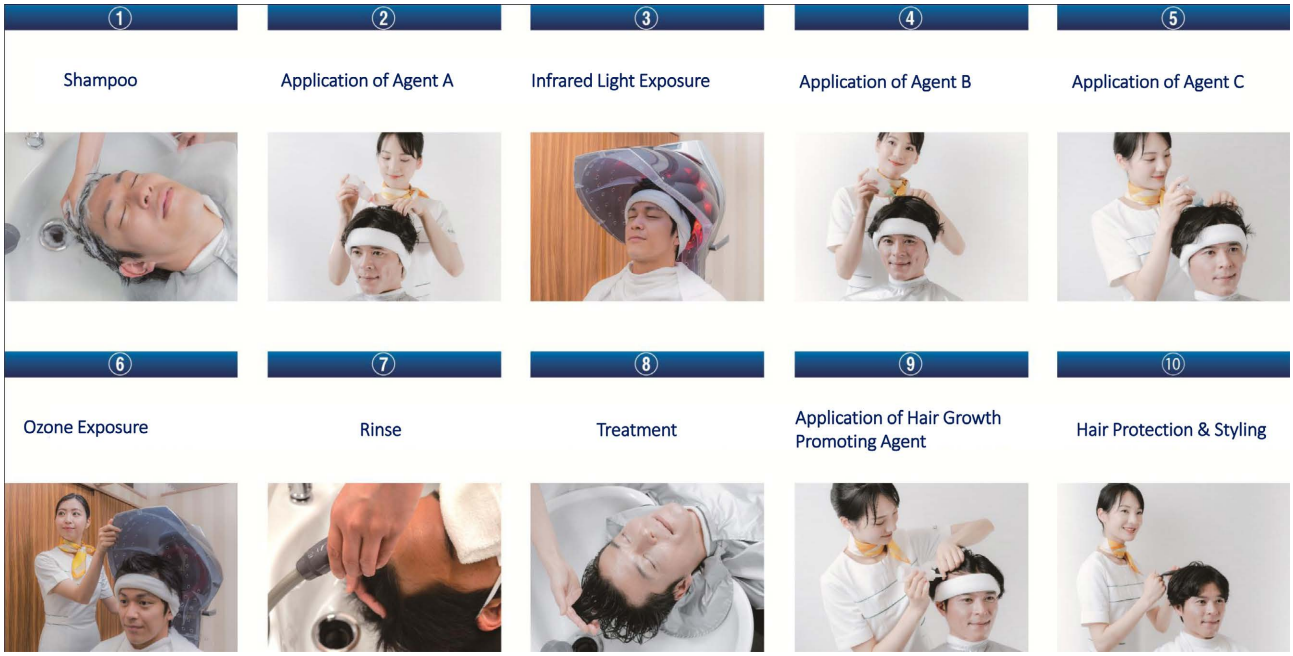


Figure 4. *α* Care Treatment Process.

Figure 5. *γ* Care Treatment Process.

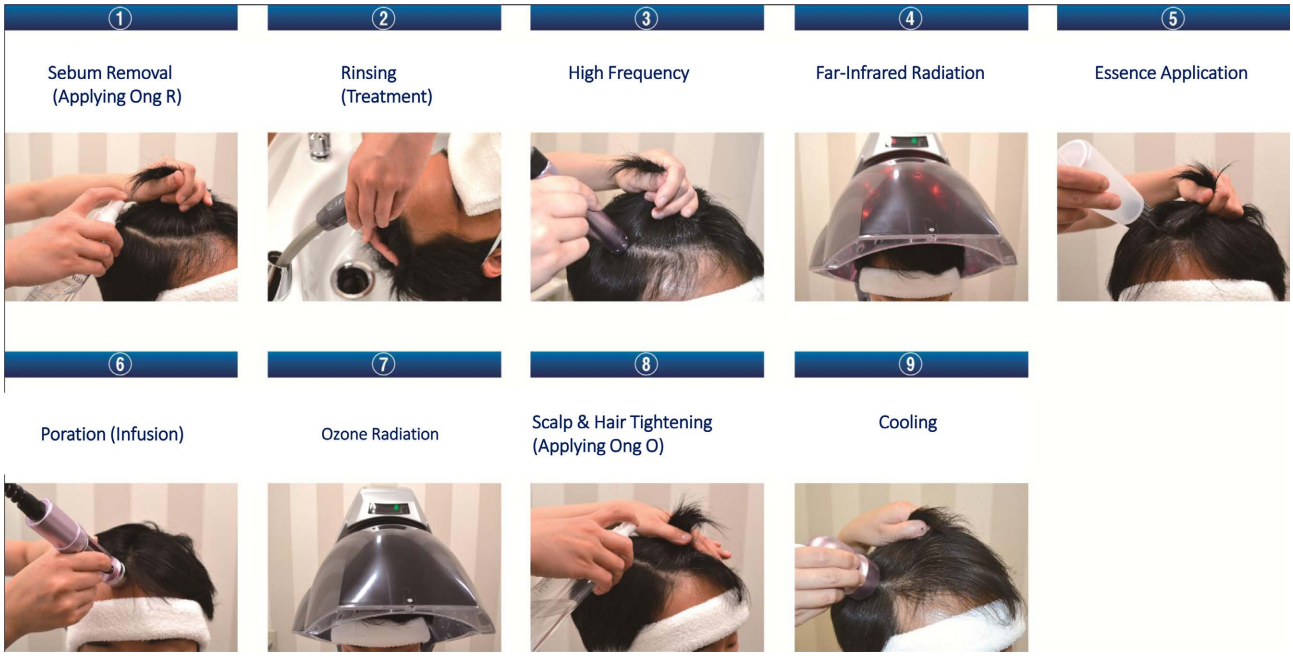


Figure 6. Poration premium care treatment process.

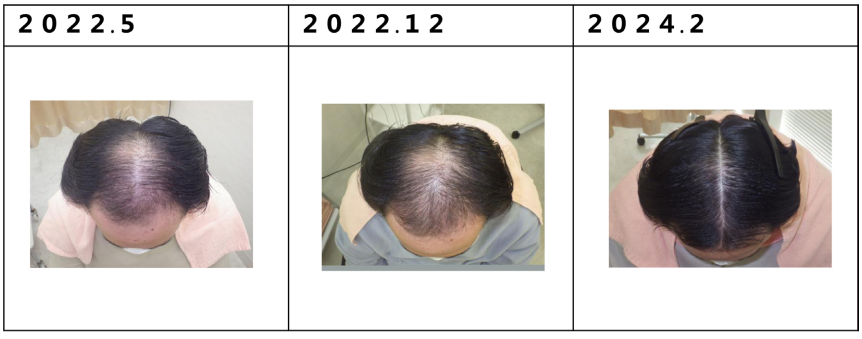
3. Results

Case photographs of subjects 1 - 11 are presented in Figures 7-17.

Subject 1: Five months after commencing treatment, oral dutasteride was started. Although no effect was observed shortly after, significant hair growth was observed on the parietal area 2 years after the start of treatment and oral medication. This was the only case involving dutasteride in the present study.

Subject 2: Two months after the start of treatment, oral finasteride and minoxidil application were started. An increase in hair volume was observed at the hairline. However, no significant difference was observed on the parietal area.

Subject 3: Two months after the start of treatment, finasteride and minoxidil were started. After 6 months, a remarkable increase in hair growth was observed

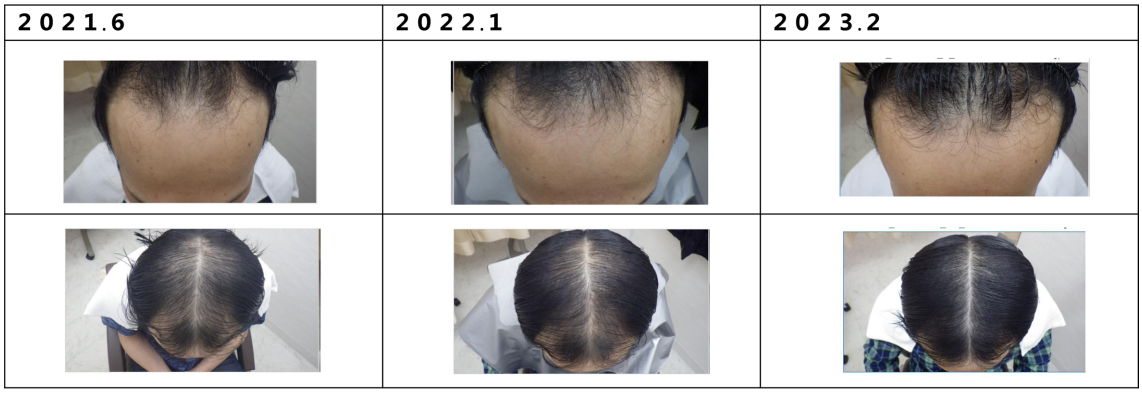


Subject 1.
Wants to increase hair growth on the top of the head. Started taking dutasteride in October 2022 and continues to take it. Currently using 《Premium》 scalp lotion β after having undergone porrification and α treatment.

Figure 7. Subject 1 clinical photograph.

Subject 2.
Wants to increase hair growth at the hairline and parietal area. Started taking finasteride and minoxidil in June 2018.Undergoing gamma, alpha, and porosity treatments and using Original Premium Scalp Shampoo and Beta.

Figure 8. Subject 2 clinical photograph.

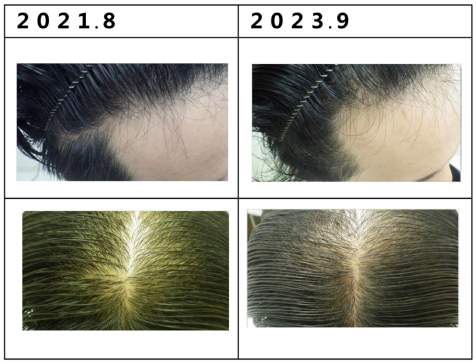


Subject 3.
Wants to increase hair growth at the hairline and parietal area. Started taking finasteride and minoxidil in August 2021.Undergoing gamma, alpha, and porosity treatments and using Premium Scalp Shampoo and Premium Beta.

Figure 9. Subject 3 clinical photograph.

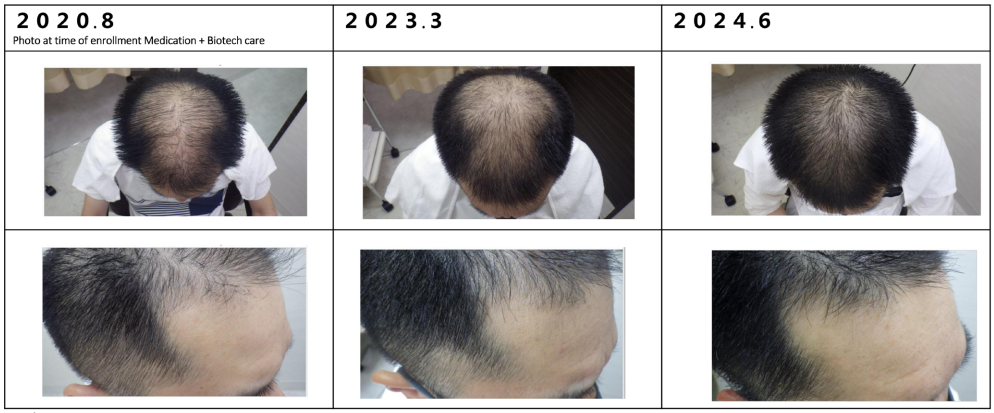
Subject 4.
Wants to increase hair growth on top of head. Started taking minoxidil in February 2017, and finasteride in September 2023, both of which she continues to take. She has undergone the “Momidashi Option + α” and “Cleansing & Shampoo Option + Polation” treatments, and has received “Premium” Scalp Shampoo, “Power” Scalp Theraputa, “Premium” Scalp Lotion β, “Plus” Scalp Essence, “Botanical Scalp lotion, 《Premium》 Scalp Accel Essence, 《Plus》 Beta Glucan, 《Plus》 Next Supplement.

Figure 10. Subject 4 clinical photograph.



Subject 5.
Wants to increase hair growth at the hairline and parietal area.
Started taking finasteride and minoxidil in October 2020 and continues to take them.
Undergoing gamma, alpha, and porosity treatments and using Original, Premium Scalp Shampoo, Beta, Step, Serum, Ong O,, R, and Tillett.

Figure 11. Subject 5 clinical photograph.



Subject 6.
Wanted to increase hair growth at the hairline and parietal area. Started taking finasteride from September 2018, but no improvement was observed. Received Gamma and Alpha treatments and used Original, Premium Scalp Shampoo, Beta, Step, Serum, and Tillette. Gradual increase in hair volume was observed when the patient started using the treatment in combination with the treatment from August 2020.Currently, an overall increase in hair volume is confirmed by the naked eye.

Figure 12. Subject 6 clinical photograph.

Subject 7.
Wants to increase hair growth on top of head.
No medication.
Received γ and α treatment, 《Premium》 scalp shampoo, 《Premium》 treatment, Premium" scalp shampoo, 'Premium' treatment, 'Premium' scalp lotion beta (single product), 'Botanical' scalp lotion (single product), 'Premium' potion mist serum, 'Plus' step supplement, 'Premium' select supplement, 'Plus' scalp cleansing, TILLET SMART-GEAR was used Cases in which hair growth on the top of the head was significantly observed in the absence of medication

Figure 13. Subject 7 clinical photograph.

Subject 8.Wants to increase hair growth on top of head. No medication. Received Momidashi and Alpha treatment and used Premium Shampoo, Premium Scalp Lotion Beta, and Brush H. Cases in which hair growth on the parietal area was significantly confirmed in the absence of medication.

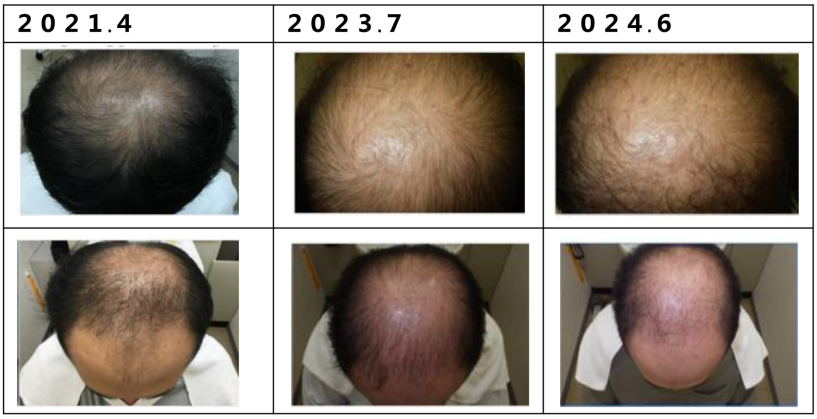
Figure 14. Subject 8 clinical photograph.

Subject 9.
Wishes to increase hair growth on the top of the head.
Dosing of α will end in October 2021.Received γ and α treatments and 《Premium》 scalp shampoo, Premium] Scalp lotion β (single product), [Botanical] Scalp lotion (single product), [Premium] Polation Mist Serum [Plus] Scalp Cleansing, and TILLET SMART-GEAR were used. Overall hair growth was confirmed to be remarkable.

Figure 15. Subject 9 clinical photograph.

Subject 10.
Wants to increase hair growth at the hairline and parietal area. No medications. Subject received [Momidashi Option + α] and used Beta, Plus Essence, Tillette, Serum, Select, Step, Accel Essence, Next, Cleansing, Avion Shampoo, and Avion Treatment. This is an example of a patient who did not get much benefit, did not have enough hair growth products, and did not have much home care

Figure 16. Subject 10 clinical photograph.



Subject 11.Wishes for overall improvement. Polation and alpha treatment. No medications being taken. Beta, Accel Essence, Step Supplement, Select Supplement, Original Supplement, and Beta Glucan were used.An example of not much benefit, and not getting any benefit from not continuing with home care.

Figure 17. Subject 11 clinical photograph.

at both the hairline and parietal area. The patient was satisfied with the results at the end of the treatment.

Subject 4: Four months after the start of treatment, the patient started minoxidil application, and improvement was confirmed at the hairline and parietal area. In September 2023, oral finasteride was started, and within a year, a marked increase in hair volume was noted. As the patient had received treatment for 8 years, no decrease in hair volume was observed during the period. This is an example of a case where a combination of oral and topical treatment significantly improved the patient's condition.

Subject 5: In this case, no significant change was observed in combination with medication use. Since hair growth was observed before taking the drug, no significant change was observed after taking the drug.

Subject 6: In this case, the patient had been taking finasteride since 2018 with no improvement; however, improvement was confirmed when combined with treatment. Individual hairs began to thicken, and overall hair growth was confirmed 4 years after the start of treatment.

Subject 7: In this case, marked hair growth was confirmed by treatment alone, without medication. The patient took great care of the hair at home and used a number of hair care products.

Subject 8: This was another case in which marked hair growth was confirmed by treatment alone, without medication. Hair growth was confirmed on the parietal area.

Subject 9: In this case, the patient started treatment in 2021 and stopped taking medication at the same time. No worsening such as hair loss due to the discontinuation of medication was observed. After 2 years of treatment, an overall increase in hair growth was observed.

Subjects 10 and 11: In these cases, no medication was taken, and no effect was confirmed by treatment alone. In both cases, at-home hair care was not continued.

4. Discussion

In this study that included 11 cases, 6 patients were taking medications along with the treatment. Various case reports have been published on the efficacy of drugs alone, and the efficacy of oral dutasteride after approximately 3 to 6 months of use has been confirmed [33]. Many studies have also reported on the efficacy of oral finasteride. However, some studies have reported on patients who did not show improvement, such as the case in this study in which no improvement was seen despite taking oral finasteride for 2 years. In the present study, a remarkable increase in hair growth was observed in Subject 6 when pore care, care to improve blood flow, and topical application of hair growth agents were combined. In folk medicine, when hair growth cannot be confirmed by taking finasteride alone, a lifestyle review is made in combination with administration of topical drugs. However, as Subject 6 was already using topical drugs, he was followed up with pore cleansing and lifestyle improvements for a few months. Consequently, we confirmed an overall increase in hair growth on the head. We also focused on the side effects of finasteride use [34]. Considering potential adverse reactions, we encouraged withdrawal from the drug, which was successful with increased hair growth in Subjects 7, 8, and 9 only by keeping the scalp clean, promoting hair growth through external drug administration, and lifestyle improvements after discontinuing the drug.

As in our study, various combination techniques aimed at promoting hair growth by integrating manual treatments and medications have been emerging. For example, Laser therapy, Hair transplantation, Off-label medications and hormonal therapies, Phytomedicine, Injectables, Exosomes, Adjuvant therapy and Camouflage techniques. In 1967, a study showed that low-level light/laser therapy (LLLT) using a ruby laser promoted hair growth in mice. LLLT devices were later FDA-cleared in 2007 for men and 2011 for women as a potential treatment for hair loss. LLLT stimulates hair growth by influencing the hair cycle using specific wavelengths between 650 nm and 1200 nm, [35] with LLLT red or near-infrared light ranging between 600 and 950 nm and fluences between 2 and 10 Joules per square centimetres (J/cm^2), over 15 - 20 minutes, 3 times a week for 6 months [36].

Recent reviews of randomized trials have found that LLLT can increase hair diameter or density compared to sham devices, with minor side effects like dry skin and scalp irritation reported. These findings support the use of LLLT as a treatment option for AGA. However, challenges exist in standardizing treatment parameters, study designs, and assessing long-term outcomes in LLLT studies [37] [38].

Hair follicle transplantation is a surgical procedure that involves removing and transplanting hair follicles from non-androgen sensitive areas to areas affected by AGA. The transplanted follicles do not miniaturize, grow in groups of 1 to 4 hairs and are harvested as units. In 2009, the FDA-approved a robotic hair restoration device to assist surgeons. Later in 2011, the ARTAS system was also approved to

harvest curly hair in black men [39]. ARTAS robotic hair transplant is a minimally invasive hair restoration system that uses artificial intelligence technology to restore hair faster and more precisely than traditional hair restoration methods.

Dutasteride is an effective off-label drug for AGA and inhibits SRD5A2 [40], and was more effective than finasteride in a meta-analysis of 24 weeks of treatment with comparable side effects [41]. In Japan and South Korea, oral dutasteride (0.5 mg/d) has been approved for male AGA [42].

Other treatment options for AGA include oral cyproterone and spironolactone, sometimes used off-label in females [43]. Cyproterone blocks the androgen receptor, while spironolactone slows androgen production by blocking androgen receptors in target tissues and decreasing testosterone production in the adrenal gland. Flutamide, a nonsteroidal antiandrogen that binds to the AR and blocks the action of testosterone, is not commonly used in the treatment of AGA in either males or females due to adverse side effects, such as liver toxicity [44] [45].

Phytomedicine, the use of plant-based products for medicinal purposes, is popular for treating AGA and can be used as a complementary or alternative treatment. Plants like Serenoa repens, Panax ginseng, Curcuma aeruginosa, Cucurbita pepo and Trifolium pratense [46]; palm extract (tocotrienol/tocopherol complex), horsetail and ashwagandha have been reported to treat AGA. Although high quality evidence from controled studies are needed these plants are reported to inhibit 5-alpha-reductase, lower cortisol levels, reduce inflammation, promote homeostasis, and maintain collagen stores [47].

Platelet-rich plasma (PRP) refers to a naturally derived mixture of platelets in a concentrated plasma solution, typically containing over 1,000,000 platelets per microliter or 2 - 7 times the concentration found in regular blood [48]. The application of PRP has been shown to stimulate hair growth, enhance cell survival, and extend the active growth phase (anagen) of the hair cycle [49]. It enhances grafting and improves follicular unit survival [50], resulting in hair density and thickness, according to recent meta-analyses of 30 articles with 687 patients using various injection methods [51]. However, the efficacy of PRP compared to other treatments for androgenetic alopecia (AGA) remains uncertain due to a lack of standardized protocols, long-term follow-up outcomes, and limited clinical evidence [52].

Mesenchymal stem cell-derived exosomes hold great promise in the field of hair restoration, as they contain cytokines and growth factors that promote hair growth [53] [54]. Research suggests that exosomes derived from dermal papilla cells can accelerate hair follicle growth, delay regression, and reduce hair loss and inflammation in preclinical models [55].

Although no clinical trials have been completed yet, anecdotal evidence and case reports suggest promising results [56] and initial studies indicate increased hair thickness and density after exosome therapy in individuals with pattern baldness [57].

A Korean pilot study showed that exosome therapy improved hair thickness (increased from 57.5 to 64.0 mm, $P \leq 0.001$) and hair density (increased from

105.4 to 122.7 counts/cm^2, $P \leq 0.001$) after 12 weeks [57] [58]. However, further research is needed to assess exosomes' biodistribution, pharmacokinetic profile, and safety [59]. Microneedling, a minimally invasive cosmetic procedure, stimulates the release of growth factors and stem cells, promoting collagen formation and improving topical treatment absorption [60], leading to improved hair density and thickness [61]. Case studies demonstrate its effectiveness when combined with therapies like PRP and minoxidil for patients unresponsive to conventional treatments, resulting in improved hair density and thickness [62]. Reported side effects include pain, bruising, and folliculitis [63].

Camouflage techniques can be helpful in disguising hair loss and boosting self-confidence [64]. These methods include temporary solutions like wigs, hair-thickening fibres, and pigmented powders, as well as semi-permanent options such as scalp micro-pigmentation, which creates the appearance of closely shaved hair follicles through tattooing [65] [66].

We believe that transient promotion of hair growth by medication is very important and can bring about satisfactory results more quickly; however, measures must be taken to prevent adverse reactions caused by long-term use of medication. We are currently developing a new theory focused on improving blood flow as a way to transiently promote hair growth by taking drugs and sustain the effect even after the patients stop taking the drugs. Conventionally, improvement of blood flow to the scalp has focused on localized and superficial treatments and external administration. In our new approach, by relaxing the fascia, which lies beneath the skin tissue, from the neck and the head, muscle stiffness and lymphatic stagnation are eliminated. In addition, blood flow to the head is stimulated, and the capillaries in the head are regenerated and renewed, allowing nutrients to be delivered to hair matrix cells to promote cell division. The theory is that by suppressing DHT and promoting IGF-1 production, while at the same time improving deep blood flow, the speed of hair growth and regrowth is accelerated. Several cases of treatment based on this theory have already been performed, and all have shown positive results. However, because at-home hair care is important in this treatment, patient cooperation and a deep knowledge of the theory of hair growth are needed for sustained effects over the long term.

5. Conclusion

A remarkable hair growth effect was confirmed by combining finasteride with our treatment. In addition, no symptoms such as hair loss were observed with continued treatment even after discontinuation of finasteride.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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