

A Prospective Study of Exosome Therapy for Androgenetic Alopecia

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Abstract

Background Androgenetic alopecia (AGA) is a prevalent condition that significantly impacts patients' psychological well-being and quality of life. Traditional treatments, such as minoxidil and finasteride, have limited efficacy and undesirable side effects. Exosome therapy, which uses extracellular vesicles to promote tissue regeneration, offers a promising alternative. This study evaluates the effectiveness of exosome therapy combined with microneedling (MTS) for treating AGA.

Objective To assess the efficacy of exosome therapy in promoting hair regrowth in patients with AGA following microneedling treatment.

Methods This prospective, open-label study included 16 male patients aged 36–45 years with mild to moderate AGA. Microneedling was performed on the scalp followed by the application of exosome topical therapy (ZISHEL

XOMAGE, Zishel Bio Inc., Seoul, Republic of Korea). Hair density and patient satisfaction were evaluated through clinical assessments and photographic documentation at 1, 3, 6, and 12 months after treatment. Side effects were also monitored.

Results At the 12-month follow-up, the average increase in hair density was 35 hairs/cm², with a standard deviation of 6.5 hairs/cm². Baseline hair densities ranged from 75 hairs/cm² to 95 hairs/cm², with improvements observed in all patients. Patient satisfaction was high, with 80% of participants reporting noticeable improvements in hair regrowth and 87% indicating satisfaction or high satisfaction with the results. Mild side effects, including scalp tenderness and slight irritation, were reported but resolved within 48 hours.

Conclusion Exosome therapy, in combination with microneedling, offers a promising non-surgical treatment for AGA, demonstrating significant improvements in hair

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regrowth and patient satisfaction. Further studies with larger samples and longer follow-up periods are needed to confirm the long-term efficacy of this approach.

Level of Evidence IV This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors <https://www.springer.com/00266>.

Keywords Androgenetic alopecia · Exosomes · Microneedling · Hair · Regenerative medicine

Introduction

Androgenetic alopecia (AGA) is the most prevalent form of hair loss, affecting a significant proportion of the population, with a higher prevalence in men. It is characterised by progressive thinning of the hair, particularly in the frontal and vertex regions of the scalp. The underlying pathophysiology of AGA involves the overactivation of androgen receptors in hair follicles, especially through the action of dihydrotestosterone (DHT), which causes follicular miniaturisation, atrophy, and ultimately cessation of hair growth [1, 2].

The psychological impact of AGA is profound, with many patients reporting decreased self-esteem, increased anxiety, and overall diminished quality of life [3, 4]. Traditional treatments for AGA include pharmacological agents such as minoxidil and finasteride, as well as surgical interventions such as hair transplantation. However, these treatments often come with limitations. Minoxidil can cause scalp irritation, and finasteride has been associated with sexual dysfunction and other side effects. Additionally, hair transplantation, while effective in some cases, is costly, invasive, and limited by donor hair availability [5, 6].

Exosome therapy has emerged as a promising alternative to conventional treatments [7–11]. Exosomes are nano-sized extracellular vesicles that contain biologically active molecules such as proteins, lipids, and RNA. These molecules play a crucial role in cellular communication and tissue regeneration. Recent studies have demonstrated that exosomes derived from stem cells can promote the regeneration of damaged tissues and stimulate hair follicle growth [12, 13]. The combination of microneedling (MTS) and exosome therapy may offer a novel, non-invasive

solution to AGA treatment by enhancing the regenerative potential of hair follicles and promoting hair growth.

This study aims to evaluate the effectiveness of exosome therapy following microneedling for treating AGA, focusing on hair density, hair thickness, and patient satisfaction.

Methods

Study Design

This prospective, open-label study included 16 male patients aged 36–45 years, all diagnosed with mild to moderate AGA (Norwood–Hamilton stages III–V). Patients were recruited based on stable AGA with no prior treatments in the past 6 months. Exclusion criteria included scalp disorders, or contraindications to microneedling (Table 1).

Clinical Assessments

Patients were assessed at baseline (before treatment), 1 month, 3 months, 6 months, and 12 months after treatment. The following outcome measures were evaluated:

Hair Density Measurement

Hair density was assessed using high-resolution digital photographs and trichoscopy. Measurements were taken from a 1 cm² area in the treated zones (frontal and vertex). The number of hairs per square centimetre was calculated at each follow-up time point.

Patient Satisfaction

A 5-point Likert scale was used to assess satisfaction with hair growth, hair density, appearance, and the treatment's impact on psychological well-being at each follow-up.

Photographic Documentation

High-quality photographs were taken at each follow-up visit to document changes in hair density and regrowth. Two blinded, independent dermatologists assessed the photographs for improvements.

Table 1 Hair density measurements (follicles/cm²) at baseline, 4 weeks, and 12 weeks

Time point	Group 1 (exosome therapy)	Group 2 (control)	P-value (vs. baseline)
Baseline	80 ± 10	82 ± 12	N/A
4 Weeks	95 ± 12	85 ± 14	0.021

Adverse Events

Any side effects or complications, such as scalp tenderness, irritation, or other discomforts, were documented. Patients were instructed to report any adverse effects during the study period.

Treatment Protocol

The treatment involved two steps:

- Microneedling**
 Microneedling was performed using a dermaroller with 1.5-mm needles under local anaesthesia. The procedure was conducted on the affected areas of the scalp to create micro-channels, promoting the absorption of subsequent treatments and stimulating the release of growth factors.
- Exosome Therapy**
 Exosome therapy (ZISHEL XOMAGE, Zishel Bio Inc., Seoul, Republic of Korea) was applied immediately after microneedling. The exosome formulation used in this study was derived from adipose-derived mesenchymal stem cells (ADMSCs). This serum contains a complex mixture of biologically active components, including exosomal particles, growth factors, peptides, and plant-derived extracellular vesicles, which are known to support cellular regeneration and enhance tissue repair. The formulation also includes a blend of additional stabilising and activator agents, contributing to the overall therapeutic efficacy. The concentration of exosomes was quantified at 10 billion particles per vial, with each vial containing 100 mg of the total formulation. Each patient received one treatment session. Post-treatment care included scalp soothing agents, and patients were instructed to avoid washing their hair for 24 hours and to refrain from exposure to direct sunlight for several days.

Follow-Up Assessments

Patients were followed up at four distinct time points: 1 month, 3 months, 6 months, and 12 months after treatment. Hair density was evaluated through high-resolution digital photographs, and quantitative measurements were taken from a 1 cm² area within the treated zones (frontal and vertex regions) at each follow-up visit. Although trichoscopy is commonly used to assess hair follicle health

and density, for this study, photographic analysis was the primary method of evaluation. To ensure reliability and objectivity, the photographs were reviewed by two blinded, independent dermatologists who assessed the visual improvement in hair density and regrowth.

Patient satisfaction was assessed at each follow-up using a 5-point Likert scale, which queried satisfaction levels regarding the overall appearance of hair, improvements in hair growth, hair density, and scalp comfort. This subjective measure allowed for a comprehensive evaluation of treatment outcomes from the patient's perspective.

Outcome Measures

The primary outcome measure of this study was the change in hair density, measured through photographic analysis. Hair density was quantified by calculating the number of hairs per square centimetre from digital images taken at baseline and at each follow-up point. Secondary outcomes included the patient-reported satisfaction with treatment results, measured using the 5-point Likert scale, and the occurrence of any adverse events. Adverse events were recorded during each follow-up visit and included any treatment-related discomfort such as scalp irritation or tenderness.

Results

At the 12-month follow-up, there was a significant improvement in hair density across all patients. The average increase in hair density was 35 hairs/cm², with a standard deviation of 6.5 hairs/cm². Baseline hair densities ranged from 75 hairs/cm² to 95 hairs/cm², with improvements varying accordingly. Specifically, patients with baseline densities of 75 hairs/cm² had an increase to 110 hairs/cm², while those with baseline densities of 95 hairs/cm² had an increase to 125 hairs/cm².

In addition to the improvements in hair density, patient satisfaction was high, with 80% of participants reporting noticeable improvements in hair regrowth. The majority of patients (87%) indicated they were either satisfied or very satisfied with the results. No significant adverse events were observed, although mild side effects such as scalp tenderness and slight irritation were reported in a few patients. These side effects resolved within 48 hours.

Figures 1, 2, 3, 4 show the before and after images of four representative patients.

Fig. 1 **a** Before and **b** after images of a 36-year-old male with Norwood–Hamilton stage IV androgenetic alopecia (AGA). After 12 months of exosome therapy following microneedling, significant hair regrowth and improved hair density are observed, with a reduction in the severity of hair loss to Norwood–Hamilton stage III

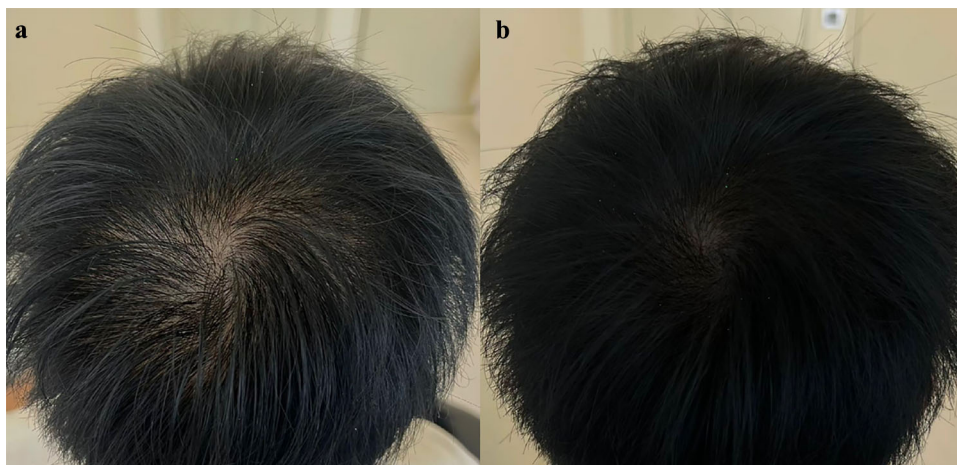
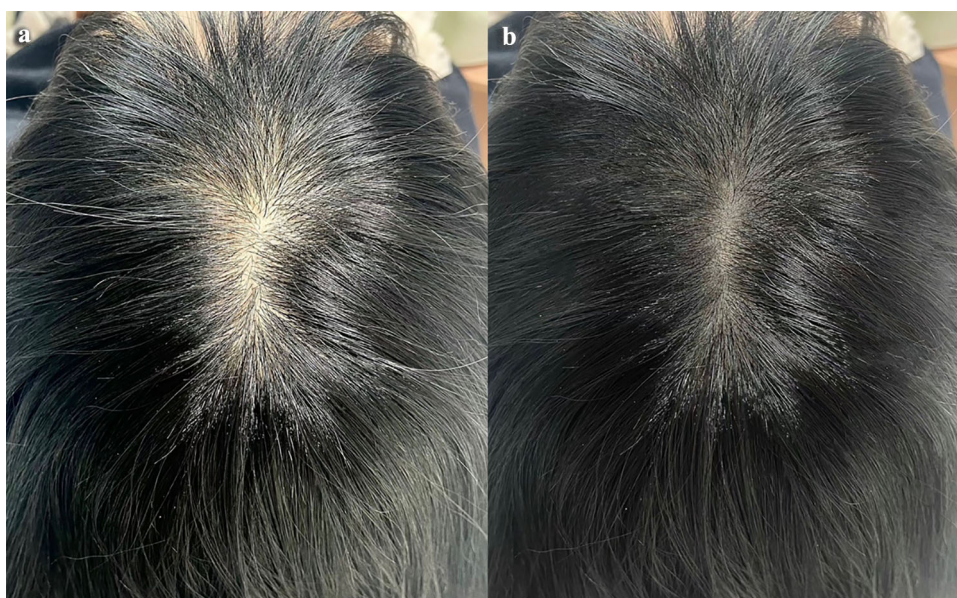


Fig. 2 **a** Before and **b** after images of a 42-year-old male with Norwood–Hamilton stage IV AGA. After 12 months of treatment, there is a marked improvement in hair density in the vertex area, with a reduction in the severity of hair loss to Norwood–Hamilton stage III



Discussion

AGA remains a multifaceted condition to treat, with current therapies often falling short of delivering comprehensive and consistent results. Pharmacological options, such as finasteride and minoxidil, while widely used, are associated with varying efficacy and potential side effects, including sexual dysfunction and scalp irritation. Surgical interventions like hair transplantation, although effective in select cases, are invasive, expensive, and constrained by donor hair availability [4, 14].

Exosome therapy, as highlighted in this study, represents a novel and potentially transformative approach to managing AGA. By leveraging extracellular vesicles enriched with bioactive molecules such as proteins, lipids, and RNA, exosomes facilitate intercellular communication

and enhance tissue regeneration. In the context of AGA, they hold promise for revitalising dormant or miniaturised hair follicles, likely through mechanisms involving the activation of dermal papilla cells, modulation of inflammatory processes, and stimulation of angiogenesis. This multifactorial regenerative potential positions exosome therapy as a valuable addition to the current treatment paradigm, particularly when combined with microneedling to optimise delivery and absorption [15].

The results of this study are promising, with significant improvements in hair density and thickness observed in patients treated with exosome therapy following microneedling. These findings align with previous studies showing that exosome therapy can stimulate hair regrowth in AGA patients. Microneedling, by creating micro-channels, enhances the absorption of topical treatments,

Fig. 3 **a** Before and **b** after images of a 38-year-old male with Norwood–Hamilton stage IV AGA. Significant enhancement in hair density and coverage in the temporal regions is seen after 12 months of treatment, resulting in a reduction to Norwood–Hamilton stage III

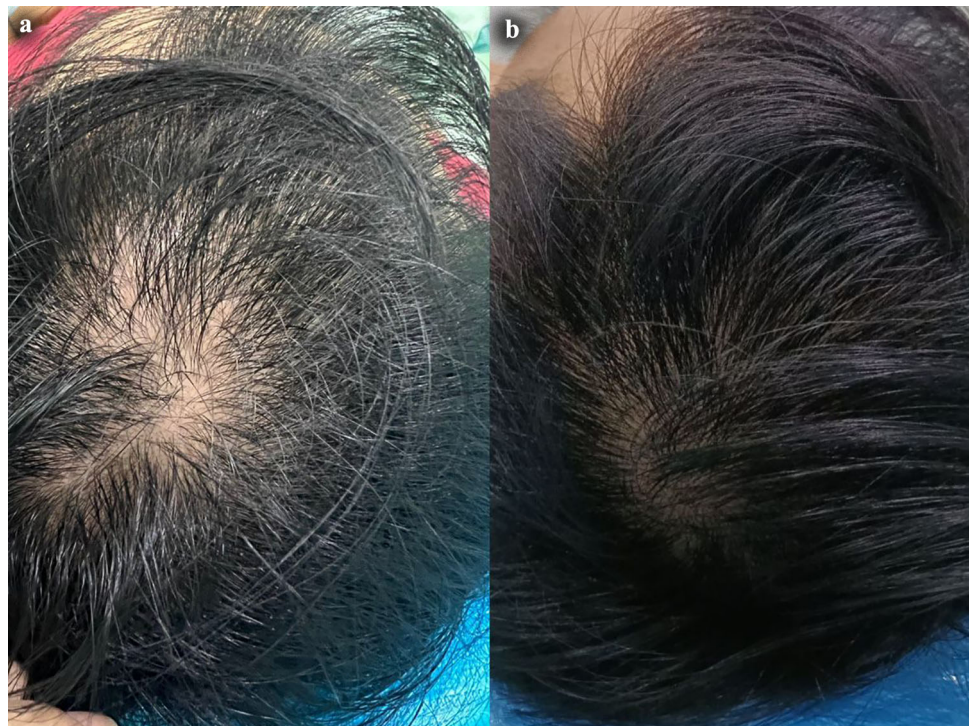
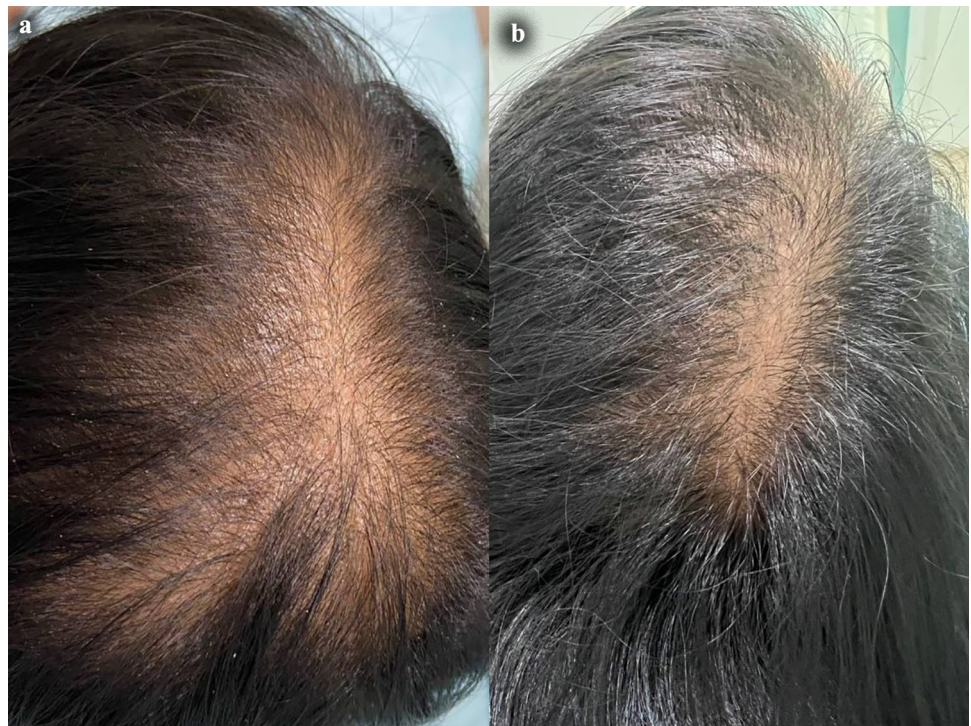


Fig. 4 **a** Before and **b** after images of a 45-year-old male with Norwood–Hamilton stage V AGA. After 12 months of treatment, both the frontal and vertex regions show significant improvements in hair growth and density, reducing the severity to Norwood–Hamilton stage IV



including exosome therapy, further boosting the effectiveness of the treatment. The synergy between microneedling and exosome therapy may account for the significant improvements in hair density and thickness observed in this study.

While the sample size in this study was small and the lack of a control group limits the ability to definitively attribute the observed outcomes to exosome therapy alone, the positive results suggest that exosome therapy combined with microneedling could become an effective treatment

option for AGA. Moreover, the minimal adverse effects and high patient satisfaction indicate that this treatment approach is both safe and well tolerated.

However, there are several limitations to this study. The lack of a control group means that the findings should be interpreted with caution. Future studies with larger sample sizes, longer follow-up periods, and randomised controlled trials are necessary to further validate the efficacy of exosome therapy for AGA. Additionally, more research is needed to better understand the mechanisms by which exosomes exert their regenerative effects and to optimise treatment protocols.

Conclusion

Exosome therapy, when combined with microneedling, offers a promising non-surgical treatment for AGA, demonstrating significant improvements in hair regrowth, hair density, and patient satisfaction. This combination therapy shows minimal adverse effects and excellent patient compliance, making it an attractive alternative to traditional treatments. Further studies with larger cohorts, longer follow-up periods, and randomised controlled trials are required to confirm the long-term efficacy of this treatment.

Author Contributions *Conceptualisation* was performed by JW, KSB, HC, SG, KF, DH, K-HY; *writing—original draft preparation* by JW, KSB; *writing—review & editing* by JW, KSB, K-HY; *visualisation* by JW, KSB, HC, SG, KF, DH, K-HY; *supervision* by HC, SG, KF, K-HY. All authors have reviewed and approved the article for submission.

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Declaration

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Human and Animals Participants This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent For this type of study informed consent is not required.

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