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LETTER TO THE EDITOR

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Rose stem cell-derived exosomes for hair regeneration enhancement via noninvasive electroporation in androgenetic alopecia

To the Editor,

Androgenetic alopecia (AGA) is the most prevalent form of alopecia, characterized by a chronic, progressive, nonscarring, and androgen-dependent condition that results in progressive follicular miniaturization. At present, the only treatments approved for AGA are topical minoxidil and oral finasteride, both of which may cause some adverse events,[1] including irritant and allergic contact dermatitis, and facial hypertrichosis from topical minoxidil,[2] and orthostatic hypotension and sexual dysfunction from oral finasteride.[3]

Exosomes, which are extracellular vesicles involved in cell communication, homeostasis, differentiation, and organogenesis, have shown potential as a promising treatment for hair morphogenesis and regeneration in AGA.[4,5] In this report, we present a case of a 54-year-old healthy male with diagnosed male pattern AGA who received exosome-based treatment with noninvasive electroporation for hair regeneration enhancement in AGA.

Herein, we describe a case involving a 54-year-old healthy male who came to our clinic complaining of hair loss. Clinical examination revealed diffuse thinning of his scalp hair and a receding hairline at the frontal and temporal regions, classified as Hamilton-Norwood Scale V, with no signs of inflammation or scarring (Figure 1A). He reported a family history of hair loss but had not undergone any previous treatments for it. Laboratory tests showed no significant findings. A diagnosis of male pattern hair loss was made. Due to the side effects of the standard treatments for AGA, including topical minoxidil solution and oral finasteride, as well as the discomfort from procedural treatments such as laser, needles, and platelet-rich plasma (PRP) methods, we discussed with the patient and opted for electroporation with exosomes as a treatment option. After obtaining informed consent, the treatment procedures were performed with the application of rose stem cell-derived exosomes (RSCEs) using electroporation, a noninvasive technique for enhancing drug delivery, thus avoiding the need for invasive procedures. A 5 mL dose of an exosome-based product (ASCE+HRLV-S from ExoCoBio Inc., Seoul, Republic of Korea), which includes 20 mg of lyophilized RSCEs and additional ingredients, was administered to the entire area of hair thinning. This was followed by electroporation (Dermashock Cool Aestech USA, California, USA), an enhanced trans-epidermal drug delivery system. The electroporation treatment lasted 15 min and was repeated every 3 weeks for a total of 12 sessions. (Figure 2).

Following the third treatment session, notable enhancements were observed in hair density, decreased hair loss, and increased hair thickness. (Figure 1B) The excellent clinical results prompted the continuation of the treatment. The patient experienced significant hair regrowth, and photographic evaluations demonstrated considerable improvements after the sixth and twelfth sessions. (Figure 1C,D) Improvements in hair regrowth were also noted 3 months after the final treatment. (Figure 1E) The dermoscopic evaluation also showed an increase in hair density and thickness. (Figure 3) The treatment was well-received and did not result in any serious adverse events.

FIGURE 1 (A) Baseline, (B) After 3rd, (C) 6th, (D) 12th treatment with exosome, electroporation, and (E) 3 months after last treatment.

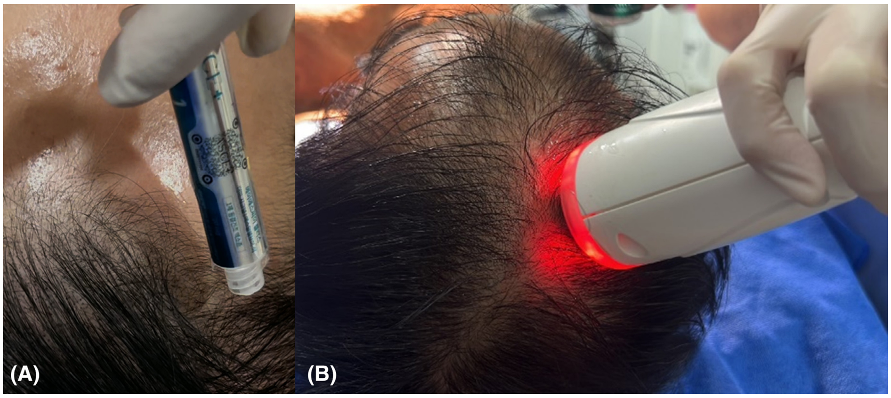

FIGURE 2 Depicts the procedure for applying exosomes to the balding scalp area (A), followed by noninvasive electroporation (B) in AGA treatment.

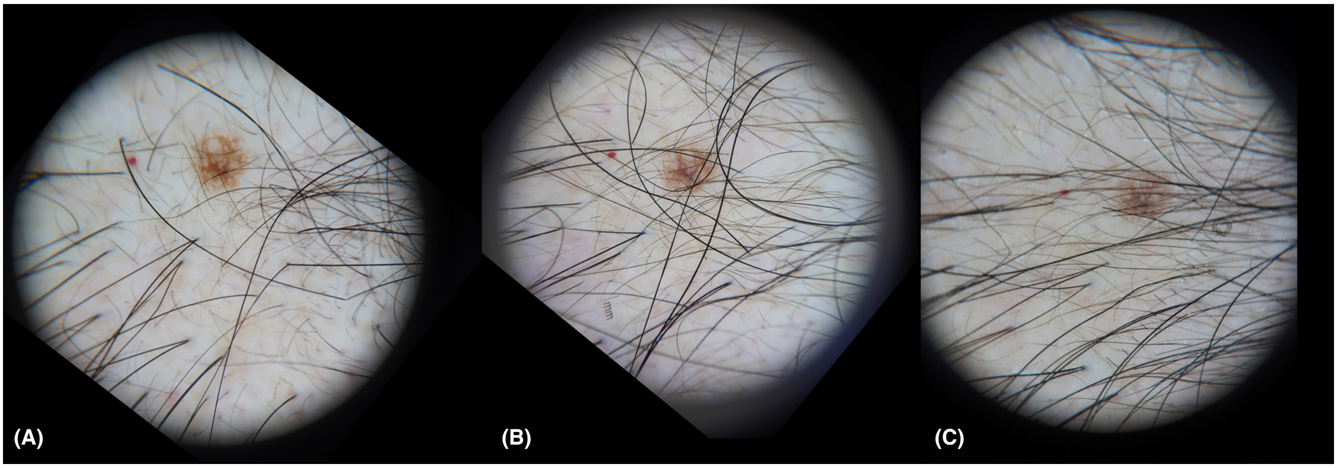

FIGURE 3 Dermoscopic examination at (A) Baseline, (B) After the 6th treatment, and (C) After the 12th treatment with exosome electroporation at the mid-scalp area, using a nevus and cherry angioma as reference points.

Exosomes have shown potential in activating the Wnt/ß-catenin signaling pathway, delivering growth factors that aid in the proliferation of dermal papilla cells, and regulating inflammation. These capabilities make them highly promising for enhancing hair regeneration.[4] The evidences of animal model studies showed milk exosomes from colostrum,[6] bone marrow–derived mesenchymal stem cells extracellular vesicles,[7] and exosomes derived from dermal papilla cells[8] to induce hair growth. The mechanisms of activation of Wnt/ß-catenin pathways rescued dihydrotestosterone-induced arrest of follicle development, protection to hair follicle cells against reactive oxygen species, leading to the increased proliferation and migration of human dermal papilla cells (HDPs), which facilitated the conversion from telogen to anagen phases in hair growth with the application of topical application, encapsulation of matrices,[9] subcutaneous injection, microneedle patches, and microneedle.[4]

In this report, we utilized RSCEs.[10] Plant cells also release exosomes or extracellular vesicles[11] similar to those produced by animal and human cells,[12] but with unique features specific to plants. Plant exosomes play crucial roles in cell-to-cell communication, intercellular signaling, stress responses, and defense mechanisms.[13]

The RSCEs isolated using tangential flow filtration and had a size range of approximately 100–200 nm, as determined by Nanoparticle Tracking Analysis and Cryo-electron microscopy.[14] Proteomic analysis revealed 206 proteins, including cell membrane components and various enzymes, alongside RNA-binding proteins. The RSCEs also contained microRNAs such as members of the Let-7 family, miR-8485, miR-574-5p, and miR-1246,[15] which play roles in inflammation regulation and cell proliferation.[16] Functionally, the RSCEs promoted growth and collagen production in human dermal fibroblasts, reduced melanin content in melanocytes, and exhibited anti-inflammatory properties in macrophages.[10]

Moreover, the roles of RSCEs for hair are explored through their effects on HDPs and their potential applications in hair health. The study found that while the crude supernatant (RSC-CM) was toxic to HDPs, the RSCEs were nontoxic. This indicates that RSCEs can be safely used on HDPs without causing cell death. Furthermore, the RSCEs were shown to enhance the growth and proliferation of these cells. The overall findings suggest that RSCEs have the potential to improve hair health by promoting the viability and growth of dermal papilla cells, which are crucial for hair follicle development and hair growth.[10]

However, FDA clearance for any injectable exosome therapy has not yet been granted, and its current use in dermatologic practice is limited to topical cosmetic application. This method is sometimes combined with microneedling or laser therapy to enhance penetration.[17,18] Additionally, there is limited clinical evidence supporting the use of exosomes for hair loss treatment, including recalcitrant alopecia through a comprehensive treatment regimen, nonablative

Er: YAG laser therapy, PRP application, and exosome.[19] Furthermore, the report investigated the repigmentation of white hair patches (poliosis circumscripta) in a patient with AGA using a combination of exosomes and fractional picosecond laser treatment.[5]

The study of micro-needling therapy combined with exosomes for ten sessions at intervals of 2–3 weeks revealed significant improvements in hair-related parameters with no serious adverse reactions.[20]

Interestingly, our findings align with a previous study that evaluated the effectiveness of adipose-derived stem cell (ASC) exosomes in treating AGA. That study involved weekly treatments combining ASC-exosomes with a micro-needle roller over 12 consecutive weeks and reported no severe adverse reactions. Patients experienced no irritation or itching; the only discomfort reported was the sensation of needle pricking during application.[21]

Therefore, a painless electroporation using a needle-free microelectrode array was utilized to improve transdermal drug delivery and enhance membrane permeability. This method opens new possibilities for introducing larger molecules into targeted tissues through the transdermal route, using the pulse electric field.[22] This could explain the efficacy of RSCEs in combination with electroporation by enhancing transepidermal drug penetration methods for AGA treatment. Moreover, these diverse application methods could present opportunities for further research and exploration in the field of exosome and hair loss treatment.

This study demonstrates the potential of RSCEs for hair regeneration via noninvasive electroporation, but several limitations need addressing. The single-case sample size limits generalizability, requiring larger-scale research for validation. The absence of a control group makes it hard to attribute effects solely to RSCEs and electroporation. Future studies should include randomized controlled trials comparing RSCEs with standard treatments like topical minoxidil. Additionally, the long-term effects and mechanisms of RSCEs were not fully explored, and their cost-effectiveness compared to existing therapies for AGA was not evaluated. Comprehensive research is essential to confirm the clinical utility of RSCEs in hair regeneration. Additionally, this pilot report demonstrates that plant stem cell-derived exosomes, an innovative biological material, can improve AGA through noninvasive delivery. Given the current limited availability of noninvasive procedures for AGA, we propose this new treatment option for patients with AGA who experience side effects from standard treatments or as an alternative noninvasive treatment option.

AUTHOR CONTRIBUTION

All authors discussed the results and contributed to the final manuscript. S.L. carried out the concept and design of study, acquisition of data or analysis, interpretation of data, drafting the article and revising it critically for important intellectual content; and B.C. and T.T. approved the version to be published.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

CONSENT

The patient signed the informed consent form after understanding the nature of the trial.

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