RESEARCH ARTICLE

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2026.2026-73
Cyprus J Med Sci 2026;11(4):315-322

Adjunctive Multimodal Therapy Incorporating Iontophoresis-Assisted Growth Factor Delivery for Hair Loss: A Real-World Retrospective Study

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Abstract

BACKGROUND/AIMS: Adjunctive multimodal therapies incorporating iontophoresis-assisted growth factor delivery have emerged as potential non-invasive treatment options for hair loss; however, real-world clinical evidence remains limited. This study evaluated the feasibility, tolerability, patient-reported hair shedding, symptom response, and treatment satisfaction associated with this treatment approach in patients with androgenetic alopecia (AGA), telogen effluvium (TE), and mixed AGA + TE.

MATERIALS AND METHODS: This single-center, retrospective, uncontrolled, real-world observational study included 46 patients who had completed a standardized four-session adjunctive multimodal treatment protocol incorporating iontophoresis-assisted growth factor delivery alongside standard-of-care management; they were selected from 78 consecutively screened individuals. Outcomes included patient-reported daily hair shedding, symptom response, procedural tolerability, and treatment satisfaction.

RESULTS: Daily hair shedding decreased significantly after treatment ($p<0.001$). After Bonferroni correction for the three diagnostic subgroup comparisons (adjusted $\alpha=0.0167$), the reduction remained statistically significant in TE ($p=0.002$), whereas AGA ($p=0.030$) and mixed AGA + TE ($p=0.025$) did not meet the corrected significance threshold. No patients remained in the ≥200 hairs/day shedding categories after treatment. Patients with TE showed greater symptom improvement than those with isolated AGA ($p=0.016$). Reduction in hair shedding was positively correlated with treatment satisfaction ($r=0.48$, $p=0.004$). No severe adverse events were documented in the medical records.

CONCLUSION: Adjunctive multimodal therapy incorporating iontophoresis-assisted growth factor delivery was associated with reduced patient-reported hair shedding and high treatment satisfaction. However, because of the retrospective, uncontrolled design, the concomitant standard-of-care therapies, and the multimodal nature of the intervention, these findings should be considered hypothesis-generating. Prospective, randomized, sham-controlled studies incorporating objective outcome measures and longer follow-up are warranted.

Keywords: Androgenetic alopecia, telogen effluvium, iontophoresis, growth factor therapy, transdermal drug delivery

INTRODUCTION

Hair loss encompasses a heterogeneous group of disorders characterized by alterations in the hair cycle and follicular dynamics. Beyond its biological dimension, hair loss is frequently associated with substantial psychosocial burden, given the central role of hair in self-perception, identity, and social interaction. Among the various causes of hair loss, androgenetic alopecia (AGA) and telogen effluvium (TE) represent the most prevalent entities in clinical practice.[1]

To cite this article: Akpınar Ü, Civaş E, Hayran Y, Fişek İzci N. Adjunctive multimodal therapy incorporating iontophoresis-assisted growth factor delivery for hair loss: a real-world retrospective study. Cyprus J Med Sci. 2026;11(4):315-322

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Received: 20.04.2026
Accepted: 15.08.2026
Publication Date: 27.08.2026

TE is characterized by a premature transition of hair follicles from the anagen (growth) phase to the telogen (resting) phase, resulting in diffuse shedding of club hairs. It is widely recognized as the most common cause of diffuse hair loss. In most cases, diagnosis is established through detailed history taking and physical examination. TE is typically a self-limited condition and lacks a standardized therapeutic approach. When an underlying trigger, such as hormonal imbalance, micronutrient deficiency (e.g., iron, zinc, or vitamin D deficiency), or metabolic disease, is identified, correction of the underlying cause generally leads to spontaneous hair regrowth.[2]

AGA, in contrast, is a non-scarring and progressive miniaturization of hair follicles occurring in genetically predisposed individuals, usually following a characteristic pattern distribution in both men and women.[3] The diagnosis is primarily clinical. Currently, topical minoxidil is Food and Drug Administration (FDA)-approved for AGA, while oral finasteride is FDA-approved for male AGA. In addition, several low-level light therapy devices have received FDA clearance for the treatment of AGA. However, numerous alternative or adjunctive approaches, including platelet-rich plasma, mesotherapy, exosomes, and growth factor-based therapies, are increasingly utilized in clinical practice. The broad spectrum of available interventions, combined with the lack of methodological standardization across studies, further complicates therapeutic decision-making.[4]

Iontophoresis is a technique that applies a low-intensity electrical current to enhance the transdermal delivery of active compounds. Experimental evidence suggests that iontophoresis using gel-based formulations can improve both *in vitro* and *in vivo* drug distribution into hair follicles. Given the cosmetic and psychological impact of alopecia, iontophoresis has been increasingly explored within dermatocosmetic applications. Topical therapies are generally preferred to systemic treatments to minimize systemic adverse effects. Nevertheless, conventional topical drug delivery is limited by the skin barrier, which may restrict drug penetration and reduce local delivery efficiency.[5] To overcome these limitations, technology-assisted delivery systems such as iontophoresis have been proposed.

The role of hair follicles as reservoirs in percutaneous drug delivery has been extensively reviewed.[6-9] Increasing attention has been directed toward follicular drug depots as a strategy for localized therapy, particularly for conditions such as acne, certain non melanoma skin cancers (e.g., Bowen's disease), and alopecia.

Among emerging approaches, the use of preformed growth factors delivered via iontophoresis has gained interest as an innovative modality. This patented technique is proposed to stimulate hair follicle activity through combined mechanisms, including the application of exogenous growth factors, microdermal scalp stimulation, pressure wave effects, and iontophoretic enhancement of transfollicular delivery.[10]

MATERIALS AND METHODS

Study Design

This was a single-center, retrospective, uncontrolled, pre-post observational cohort study evaluating an adjunctive multimodal therapy incorporating iontophoresis-assisted growth factor delivery for hair loss. This retrospective study included patients who underwent treatment between January 1, 2025, and January 1, 2026. Owing to its retrospective and uncontrolled design, this study was intended to evaluate real-world feasibility, tolerability, and patient-reported outcomes rather than to establish a causal treatment effect. Accordingly, the findings should be interpreted as hypothesis-generating rather than confirmatory evidence of treatment efficacy.

Patient Selection

Medical records of 78 consecutive patients who underwent adjunctive multimodal therapy incorporating iontophoresis-assisted growth factor delivery during the study period were retrospectively reviewed.

Patients were eligible if they completed the planned four-session treatment protocol and had adequate baseline and post-treatment clinical documentation.

Patients were excluded if they did not complete the planned four-session treatment protocol or had missing or incompatible diagnostic information. Of the 78 patients screened, 18 did not complete the planned four-session treatment protocol, 14 had missing diagnostic information, and 2 had diagnoses incompatible with the study eligibility criteria (frontal fibrosing alopecia and trichotillomania). Two patients had both missing diagnostic information and incomplete treatment; therefore, the exclusion categories were not mutually exclusive. Overall, 32 unique patients were excluded and 46 were included in the final analysis.

Diagnostic Assessment

All patients underwent a standardized dermatologic evaluation, including clinical examination and trichoscopy, performed by a dermatologist before treatment initiation.

The diagnosis of AGA was established based on characteristic clinical findings together with trichoscopic evidence of follicular miniaturization.

The diagnosis of TE was established using clinical history, hair-pull test findings, trichoscopic examination, laboratory investigations when clinically indicated, and assessment of potential triggering factors, including nutritional deficiencies, systemic diseases, medications, and recent physiological or psychological stressors.

Patients presenting with clinical features of both disorders were classified as having mixed AGA and TE.

Device and Procedure

Skin Patting® (aPS, Faenza, Ravenna, Italy) is a patented device designed to stimulate hair follicle activity through a multimodal approach combining controlled microdermal stimulation, radial pressure wave application, and iontophoresis-assisted transdermal delivery.

No anesthesia was required during the procedure.

The treatment protocol began with controlled microdermal stimulation of the affected scalp areas using a needle length of 0.25 mm. Microperforations were applied in longitudinal, vertical, and diagonal directions, with eight passes in each direction or until mild erythema was achieved, which was considered the procedural endpoint. This controlled stimulation was intended to activate the dermal repair cascade, including increased vascularization, increased fibroblast proliferation, and enhanced collagen and elastin synthesis.

The device simultaneously generated radial pressure waves directed toward the scalp. This mechanical action was designed to support microcirculation, stimulate cellular metabolism, and facilitate uptake of active compounds.

Subsequently, iontophoresis was applied to enhance transdermal penetration of the topical formulation. This electrical stimulation was intended to promote transfollicular delivery by increasing skin permeability and supporting the absorption of bioactive ingredients. Iontophoresis and LED exposure were delivered using the device's standardized preset protocol, according to the manufacturer's specifications.

At the end of each session, the scalp was exposed to red LED light to provide additional biostimulatory support. Each treatment session lasted approximately 20-25 minutes.

Treatment sessions were performed at 3-week intervals, resulting in a total treatment duration of approximately 9 weeks. Clinical outcomes were evaluated immediately after completion of the fourth treatment session.

Composition of the Topical Gel

The topical gel used in this study consisted of bioactive peptides, carrier agents, and stabilizing components formulated to support follicular activity and facilitate transdermal delivery.

Bioactive Components

The formulation included the following peptides: octapeptide-2, a growth factor-like peptide involved in cellular signaling and follicular activation; copper tripeptide-1 (Glycyl-L-Histidyl-L-Lysine-Copper), an angiogenic and reparative peptide associated with dermal papilla activation, vascular support, and extracellular matrix remodeling; sh-oligopeptide-1, an epidermal growth factor analogue promoting cellular proliferation; sh-oligopeptide-2, an insulin-like growth factor-1 (IGF-1) analogue implicated in follicular growth and anagen phase support; and sh-polypeptide-1 and sh-polypeptide-3, recombinant growth factor analogues associated with cellular metabolism and microenvironment modulation.

Carriers and Penetration Modulators

Hydroxyethylcellulose served as the gel matrix to ensure uniform distribution and controlled release. Glycerin functions as a humectant, enhancing stratum corneum hydration and facilitating penetration. Hydrogenated lecithin acted as a lipid-based carrier to improve membrane compatibility and enhance transdermal transport. Glycine soja (soybean) oil provided lipophilic support with antioxidant properties, while sodium oleate functioned as an emulsifying and penetration-enhancing agent.

Stabilizing Components

Phenoxyethanol and imidazolidinyl urea were included as antimicrobial preservatives, and disodium EDTA served as a chelating agent to enhance formulation stability.

The procedure was used as an adjunct to standard-of-care management (e.g., topical minoxidil for AGA and etiologic management for TE), reflecting routine clinical practice.

Patients with AGA were routinely prescribed topical minoxidil unless contraindicated. Patients with documented iron or vitamin D deficiency received appropriate replacement therapy according to routine clinical practice. Therefore, the observed outcomes reflect the combined effect of standard-of-care management and the adjunctive multimodal intervention, and should not be interpreted as the isolated effect of iontophoresis-assisted growth factor delivery.

Outcome Assessment

No predefined long-term follow-up protocol was available due to the retrospective design of the study. Outcome measures included patient-reported daily hair-shedding categories, accompanying scalp symptoms, procedural pain, and overall treatment satisfaction. Hair shedding was assessed by asking patients to estimate the number of hairs shed per day during routine clinical evaluation. Based on predefined investigator-assigned categories, responses were classified as <100, 100-200, 200-300, or >300 hairs/day. No validated questionnaire or standardized hair-counting method was used. Because this was a retrospective real-world study, outcome assessments reflected routine clinical practice rather than a standardized research protocol. Procedural pain was assessed at the end of the fourth treatment session using a 10-point visual analogue scale (VAS), where 0 indicated no pain and 10 indicated the worst imaginable pain. Overall treatment satisfaction was evaluated after completion of the treatment protocol using a 5-point Likert scale (1= very dissatisfied; 5= very satisfied). Adverse events were actively assessed and documented at each treatment session.

This study was approved by the Bahçeşehir University Non-Interventional Clinical Research Ethics Committee (approval number: 2026-01/06, date: 07.01.2026). The study was conducted in accordance with the principles of the Declaration of Helsinki. The evaluated treatments had been performed as part of routine clinical practice. Ethics approval was obtained prior to the retrospective review of the medical records and data analysis. Written informed consent was obtained from all patients prior to treatment. As this was a retrospective review of routinely collected clinical data, no additional consent was required for data analysis.

Statistical Analysis

All statistical analyses were performed using SPSS for Windows (IBM Corp., Armonk, NY, USA; version 23.0). Categorical variables were expressed as frequencies and percentages. Differences between independent categorical variables were evaluated using the chi-square test or Fisher's exact test, as appropriate. Because of the small cell counts, the comparison of symptom response categories between diagnostic groups was performed using Fisher's exact test. The distribution of continuous variables was assessed using histograms and the Kolmogorov-Smirnov test. Normally distributed variables were presented as mean ± standard deviation, whereas non-normally distributed variables were expressed as median interquartile range (IQR). Comparisons of independent continuous variables were performed using the Student's t-test or the Mann-Whitney U test, as appropriate. Changes in daily hair shedding before and after treatment were analyzed using the Wilcoxon signed-rank test. Of the 46 patients, 45 had baseline shedding data and 44 had post-treatment data; therefore, only 44 patients had both measurements recorded and were included in the paired Wilcoxon signed-rank analysis. For correlation analyses, the reduction in hair-shedding was calculated as the ordinal difference between baseline and post-treatment hair-shedding categories (baseline category - post-

treatment category), with larger positive values indicating greater improvement. Correlation analyses were performed using Spearman's correlation coefficient. To account for multiple comparisons across the three diagnostic subgroup analyses (TE, AGA, and combined AGA + TE), a Bonferroni correction was applied, yielding an adjusted significance threshold of α=0.0167 (0.05/3). For all other analyses, a two-tailed p-value <0.05 was considered statistically significant. Due to the retrospective design, some variables were incompletely documented; denominators are therefore reported where applicable.

RESULTS

Patient Characteristics

During the study period, the medical records of 78 consecutive patients who underwent adjunctive multimodal therapy incorporating iontophoresis-assisted growth factor delivery were screened for eligibility. 18 patients did not complete the planned four-session treatment protocol; 14 had missing diagnostic information; and 2 had diagnoses that were incompatible with the study eligibility criteria (frontal fibrosing alopecia and trichotillomania). Two patients had missing diagnostic information and incomplete treatment. Thus, 32 unique patients were excluded and 46 were included in the final analysis. A flow diagram illustrating patient screening, reasons for exclusion, and inclusion in the study is presented in Figure 1.

The baseline characteristics of the study population are summarized in Table 1. A total of 46 patients were included in the analysis. The mean age was 33.3±9.9 years, and the mean body mass index (BMI) was 23.6±4.3 kg/m^2. Diagnostic information was available for 45 patients.

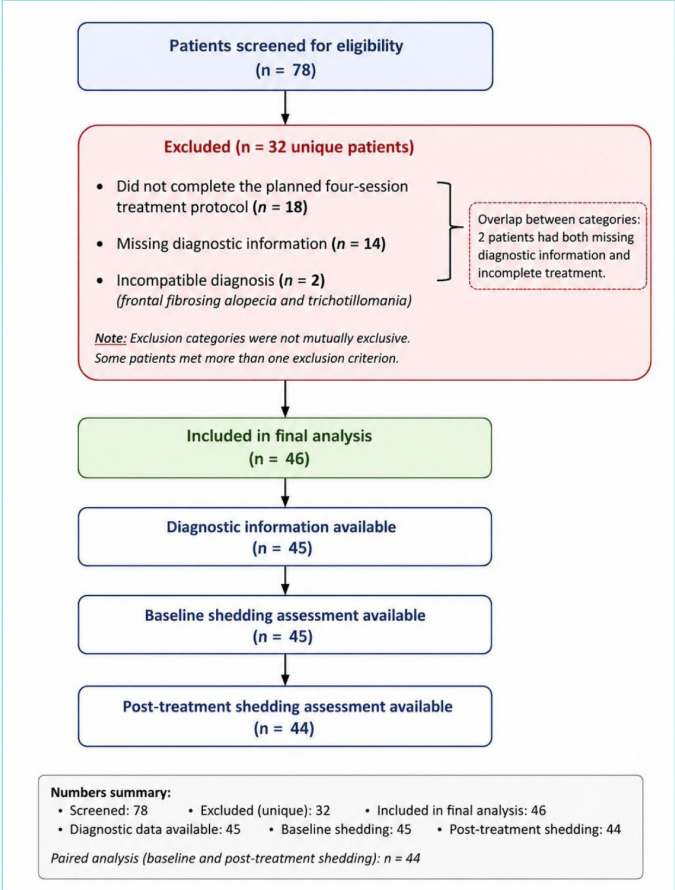

Figure 1. Flow diagram of patient selection and study inclusion.

Changes in Daily Hair Shedding

Baseline shedding data were available for 45 patients and post-treatment data for 44 patients. Paired baseline and post-treatment measurements, required for the Wilcoxon signed-rank test, were available for 44 patients. Missing baseline or post-treatment shedding data reflected incomplete documentation in routine clinical records, rather than protocol-defined exclusions.

Changes in patient-reported daily hair shedding before and after treatment are summarized in Table 2. Among the 44 patients with paired measurements, patient-reported daily hair shedding decreased significantly following treatment (Wilcoxon signed-rank test, Z=-4.318, p<0.001, r=0.65), indicating a large effect size. After applying the Bonferroni correction for the three diagnostic subgroup comparisons (adjusted α=0.0167), the decrease in hair shedding remained statistically significant in the TE subgroup (n=15, Z=-3.169, r=0.82, p=0.002), whereas the decreases observed in the AGA (n=19, Z=-2.165, r=0.50, p=0.030) and combined AGA + TE (n=9, Z=-2.236, r=0.75, p=0.025) subgroups did not meet the Bonferroni-adjusted significance threshold, although both were statistically significant at the unadjusted α=0.05

Table 1. Baseline characteristics of the study population

Characteristic	Value
Overall sample (n=46)	
Age (years), mean ± SD	33.3±9.9
Female sex, n (%)	25 (54.3)
Male sex, n (%)	21 (45.7)
Height (cm), mean ± SD	170.6±10.6
Weight (kg), mean ± SD	72.9±18.7
Body mass index (kg/m^2), mean ± SD	23.6±4.3
Diagnosis (n=45), n (%)*	
Androgenetic alopecia (AGA)	20 (44.4)
Telogen effluvium (TE)	15 (33.3)
AGA + TE	10 (22.2)
Family history of hair loss, n (%)	37 (80.4)
Current smoker, n (%)	11 (23.9)
Alcohol consumption, n (%)	10 (21.7)
Presence of systemic disease, n (%)	12 (26.1)
Systemic medication use, n (%)	20 (43.5)
Daily hair shedding before treatment (n=45), n (%)	
<100 hairs/day	15 (33.3)
100-200 hairs/day	23 (51.1)
200-300 hairs/day	4 (8.9)
>300 hairs/day	3 (6.7)
Presence of scalp symptoms (n=46), n (%)	
Any scalp symptom	15 (32.6)
Pain	4 (8.7)
Itching	11 (23.9)

*Diagnostic information was available for 45 patients; percentages for diagnostic categories were calculated using the number of patients with available diagnostic data.
SD: Standard deviation.

Table 2. Distribution of patient-reported daily hair shedding categories before and after treatment according to diagnosis

Hair shedding category	Baseline	After 4th session
Overall (n=44), p<0.001		
<100 hairs/day	15 (34.1)	36 (81.8)
100-200 hairs/day	22 (50.0)	8 (18.2)
200-300 hairs/day	4 (9.1)	0
>300 hairs/day	3 (6.8)	0
Androgenetic alopecia (AGA) (n=19), p=0.030		
<100 hairs/day	11 (57.9)	17 (89.5)
100-200 hairs/day	5 (26.3)	2 (10.5)
200-300 hairs/day	3 (15.8)	0
>300 hairs/day	0	0
Telogen effluvium (TE) (n=15), p=0.002		
<100 hairs/day	1 (6.7)	11 (73.3)
100-200 hairs/day	10 (66.7)	4 (26.7)
200-300 hairs/day	1 (6.7)	0
>300 hairs/day	3 (20.0)	0
AGA + TE (n=9), p=0.025		
<100 hairs/day	3 (33.3)	8 (88.9)
100-200 hairs/day	6 (66.7)	1 (11.1)
200-300 hairs/day	0	0
>300 hairs/day	0	0

Values are presented as n (%). Percentages were calculated using the number of patients with paired baseline and post-treatment assessments in each group. Hair shedding before and after treatment was compared using the Wilcoxon signed-rank test. For the three diagnostic subgroup comparisons, a Bonferroni correction was applied, with an adjusted significance threshold of α=0.0167; reported p-values are unadjusted.

level. Patients without documented diagnostic classification (n=1) were excluded only from the diagnosis-based subgroup analyses and were included in the overall paired analysis. Notably, no patients remained in the ≥200 hairs/day categories after treatment.

These findings indicate a consistent reduction in daily hair shedding reported by patients following the adjunctive multimodal treatment protocol in this real-world clinical cohort.

Symptom Response

Baseline scalp symptoms, symptom response after treatment, procedural pain, treatment satisfaction, and adverse events are summarized in Table 3.

Symptom response was analyzed separately from patient-reported hair shedding, to distinguish subjective symptom improvement from changes in shedding. Patients with TE (n=8) demonstrated significantly greater symptom improvement compared with patients with isolated AGA (n=7) (Fisher's exact test, p=0.016).

No statistically significant associations were observed between symptom response and age, sex, BMI, smoking status, alcohol consumption, systemic disease, medication use, family history of hair loss, or baseline shedding category (all p>0.05).

Table 3. Patient-reported outcomes following adjunctive multimodal therapy

Outcome	Result
Baseline scalp symptoms (n=46), n (%)	
Any scalp symptom	15 (32.6)
Pain	4 (8.7)
Itching	11 (23.9)
Symptom response among symptomatic patients (n=15), n (%)	
No improvement	3 (20.0)
Partial improvement	10 (66.7)
Complete improvement	2 (13.3)
Procedural pain at the end of the fourth session (VAS, 0-10; n=46), median (IQR)	5 (2-7)
Treatment satisfaction (5-point Likert scale) (n=46), n (%)	
1 (very dissatisfied)	3 (6.5)
2	1 (2.2)
3	8 (17.4)
4	22 (47.8)
5 (very satisfied)	12 (26.1)
Adverse events	
Severe adverse events	None documented

Values are presented as n (%) unless otherwise stated. Pain was assessed using a 10-point visual analogue scale (VAS). Treatment satisfaction was assessed using a 5-point Likert scale. Symptom response was evaluated only in patients reporting baseline scalp symptoms (n=15). No severe adverse events were documented in the medical records. IQR: Interquartile range.

Pain During Treatment

Procedural pain and adverse events are summarized in Table 3. Procedural pain was assessed in 46 patients at the end of the fourth treatment session. The median VAS pain score was 5 (IQR, 2-7). No severe adverse events were documented in the medical records.

Patient Satisfaction

Treatment satisfaction scores are summarized in Table 3.

A moderate positive correlation was observed between the reduction in daily hair shedding and patient satisfaction (Spearman's correlation test, n=44, r=0.48, p=0.004), indicating that greater perceived clinical improvement was associated with higher satisfaction levels.

Age showed a weak negative correlation with satisfaction (r=-0.25), which did not reach statistical significance (p=0.098; Spearman's correlation test, n=46). Satisfaction was not significantly associated with sex, BMI, smoking status, alcohol consumption, systemic disease, medication use, family history of hair loss, baseline shedding, or baseline symptom presence (all p>0.05).

DISCUSSION

Non-invasive transdermal delivery is limited by the barrier function of the stratum corneum; however, iontophoresis enhances the penetration of hydrophilic and charged molecules through low-intensity electrical current.[11] In the context of hair disorders, this approach may increase the follicular bioavailability of topically applied bioactive compounds.

Experimental studies support this mechanism. Gelfuso et al.[12] demonstrated significantly greater follicular accumulation of minoxidil sulphate with iontophoresis compared to passive delivery, with findings further supported by *in vivo* evidence. Additional studies have shown that combining optimized formulations with iontophoresis enhances follicular targeting.[12,13]

Clinical investigations have reported improvements in hair density and diameter following growth factor-based therapies delivered via iontophoresis and in split-scalp designs where iontophoresis enhanced transdermal absorption of growth factor cocktails.[10,14] Similarly, favorable outcomes and high tolerability have been reported with iontophoresis-assisted adjunctive protocols.[15]

Against this background, in this real-world retrospective cohort, daily hair shedding significantly decreased after four sessions ($p<0.001$). After Bonferroni correction for the three diagnostic subgroup comparisons (adjusted $\alpha=0.0167$), the reduction remained statistically significant in the TE subgroup ($p=0.002$), whereas the reductions observed in the AGA ($p=0.030$) and combined AGA + TE ($p=0.025$) subgroups did not meet the corrected significance threshold. Notably, no patients remained in the ≥200 hairs/day categories post-treatment. Although shedding categories represent patient-reported outcomes, the overall reduction and the direction of change observed across diagnostic subgroups suggest a pattern of improvement. A reduction in patient-perceived daily hair shedding may represent an important early treatment outcome, even in the absence of objective evidence of hair regrowth. Excessive hair shedding is one of the most common reasons patients seek medical attention, and is frequently associated with anxiety and a reduced quality of life. Therefore, a perceived reduction in shedding may improve patients' reassurance, treatment adherence, and overall satisfaction; however, these subjective findings should be interpreted cautiously until confirmed by objective assessments. However, because the study lacked a control or sham-treated group, these changes cannot be attributed solely to iontophoresis-assisted growth factor therapy.

The intervention evaluated in this study consisted of a standardized multimodal protocol that included controlled microdermal stimulation, radial pressure waves, iontophoresis-assisted delivery of a growth-factor-containing gel, and red-LED exposure. Consequently, the observed clinical improvements should not be attributed to any individual component of the protocol, including iontophoresis, but should rather be interpreted as the overall effect of the combined adjunctive intervention delivered in routine clinical practice.

While classical AGA is primarily characterized by progressive follicular miniaturization rather than pronounced daily shedding, increased hair shedding is commonly reported in routine clinical practice, particularly in early-stage disease or in mixed phenotypes such as AGA combined with TE. Therefore, changes in patient-reported shedding categories in our cohort should be interpreted within this clinical context rather than as a direct surrogate marker of hair regrowth. In addition, the natural course of TE, which may improve spontaneously after correction of triggering factors or over time, should be considered when interpreting the reduction in shedding observed in TE patients.

Moreover, because all patients received standard-of-care management according to their underlying diagnosis, including topical minoxidil for AGA and correction of reversible causes of TE when indicated, the relative contribution of the adjunctive multimodal intervention cannot be determined in the absence of a comparator group.

Symptom improvement was analyzed separately from reduction in shedding. Patients with TE demonstrated greater symptom improvement than those with isolated AGA, potentially reflecting underlying pathophysiologic differences. A moderate correlation between shedding reduction and patient satisfaction ($r=0.48$, $p=0.004$) indicates that perceived clinical improvement translates into meaningful patient benefit. Nevertheless, patient-reported outcomes are susceptible to recall bias and expectation effects, particularly in uncontrolled real-world studies.

The observed clinical findings are biologically plausible, as growth factor-based interventions have been shown to promote hair regeneration and anagen-related gene expression, and data have identified IGF-1 as an important regulator of follicular growth.[16,17] Multiple growth factors involved in follicular cycling and microenvironment modulation have been described.[18] Our peptide-rich formulation aligns with this regenerative framework.

Our findings are consistent with prior regenerative topical and growth factor-based studies reporting reduced shedding and improved hair parameters.[1,19,20] Across these modalities, enhanced follicular delivery appears central to clinical improvement.

The present study reflects routine clinical practice in which iontophoresis-assisted growth factor therapy was applied as an adjunct to standard management. While this design limits the ability to isolate of its independent effect, the overall reduction in patient-reported shedding, favorable tolerability profile, and association between clinical response and satisfaction provide supportive real-world evidence suggesting the feasibility of this adjunctive approach in hair loss management.

Study Limitations

Several limitations should be acknowledged. The retrospective design and absence of a control or sham-treated group preclude causal inference and limit the ability to account for placebo effects or regression to the mean. In addition, only patients who completed the planned four-session treatment protocol and met the eligibility criteria were included in the final analysis. Consequently, attrition and completer bias cannot be excluded, and treatment tolerability, patient satisfaction, and favorable patient-reported outcomes may have been overestimated. The intervention was administered alongside standard-of-care treatments, including topical minoxidil in AGA and etiologic management in TE, which limited the ability to isolate the independent contribution of iontophoresis-assisted therapy. In addition, detailed patient-level data regarding micronutrient supplementation were not consistently available. Furthermore, this was a single-center study with a relatively small and clinically heterogeneous sample, including patients with AGA, TE, and mixed AGA + TE. These characteristics may limit the external validity (generalizability) of the findings to other patient populations, clinical settings, or treatment protocols. In addition, the relatively small sample size within diagnostic subgroups reduced statistical power for subgroup analyses. Missing data for some variables may also introduce selection bias.

In addition, objective outcome measures, such as standardized global photography, phototrichograms, hair density measurements, hair shaft diameter analysis, and blinded trichoscopic assessments, were

not available. Consequently, treatment response relied primarily on patient-reported outcomes, which are inherently susceptible to recall and expectation biases. Furthermore, clinical outcomes were assessed only immediately after the fourth treatment session; therefore, the durability of the observed improvements remains unknown.

Nevertheless, the observed reduction in patient-reported hair shedding and its association with treatment satisfaction support the feasibility of this adjunctive multimodal approach in routine clinical practice and justify further prospective evaluation. These findings should therefore be interpreted as real-world observational evidence supporting feasibility rather than definitive evidence of therapeutic efficacy.

CONCLUSION

Adjunctive multimodal therapy incorporating iontophoresis-assisted growth factor delivery was associated with improvements in patient-reported hair shedding and treatment satisfaction among patients in this real-world retrospective cohort who completed the treatment protocol. Although the retrospective, uncontrolled design and concomitant standard therapies preclude attribution of an independent treatment effect, these findings support the feasibility of incorporating this adjunctive multimodal treatment protocol into routine clinical practice.

Prospective, randomized, sham-controlled studies incorporating objective outcome measures, including standardized global photography, blinded trichoscopic assessment, phototrichogram-derived hair density, and hair-shaft diameter measurements, and longer follow-up, are warranted to determine the independent therapeutic contribution of iontophoresis-assisted growth factor delivery within this multimodal treatment protocol.

MAIN POINTS

- Adjunctive multimodal therapy incorporating iontophoresis-assisted growth-factor delivery was associated with a significant overall reduction in patient-reported daily hair shedding; after Bonferroni correction, the reduction remained statistically significant in the telogen effluvium subgroup.
- After four sessions, no patients remained in the ≥200 hairs/day shedding categories, indicating a favorable change in patient-reported hair shedding.
- A reduction in patient-reported hair shedding correlated with higher treatment satisfaction, which supports the clinical relevance of this adjunctive multimodal approach in real-world practice.

ETHICS

Ethics Committee Approval: The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Bahçeşehir University Non-Interventional Clinical Research Ethics Committee (approval number: 2026-01/06, date: 07.01.2026).

Informed Consent: Written informed consent was obtained from all participants prior to treatment. Due to the retrospective design of the study, no additional consent was required for data analysis.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ü.A., E.C., Concept: Ü.A., E.C., N.F.İ., Design: Ü.A., E.C., Y.H., N.F.İ., Data Collection and/or Processing: Ü.A., Y.H., Analysis and/or Interpretation: Ü.A., Y.H., Literature Search: Ü.A., Y.H., N.F.İ., Writing: Ü.A., Y.H.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors. The device manufacturer had no role in the study design, data collection, data analysis, manuscript preparation, or the decision to submit the manuscript for publication. The authors have no financial or commercial relationship with the manufacturer of the device evaluated in this study.

Financial Disclosure: The authors declared that this study received no financial support.

Declaration on the Use of Artificial Intelligence (AI): Artificial intelligence has been used to assist with "text editing".

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