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ORIGINAL ARTICLE

Clinical study on the efficacy and tolerability of a topical regenerative treatment in patients with telogen effluvium and mild androgenetic alopecia

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Abstract

Hair loss may change the quality of life since modern society considers hair an essential element in beauty definition. The most common causes of hair loss are androgenetic alopecia (AGA) and telogen effluvium (TE). AGA requires a lifetime use of minoxidil or finasteride (and sometimes they lose efficacy over the years), whereas TE has no standardized therapy available. Our study focuses on a novel topical regenerative preparation that, by mimicking autologous PRP, can safely and efficiently improve hair loss in patients affected by TE and AGA.

KEYWORDS
androgenetic alopecia, growth factors, hair loss, PRP, telogen effluvium

1 | INTRODUCTION

Alopecia is a clinical condition characterized by a variable alteration of the hair. Hair loss may have a negative impact on the personal life since modern society considers hair an essential element in beauty definition.

Hair loss could be associated to different clinical conditions: some of them are widely spread, such as androgenetic alopecia (AGA), which is the most common cause of hair loss. The onset may be at any age after puberty and the frequency increases with age. The pathogenesis of AGA shows a crucial role played by androgens on the follicles. The disease is characterized by a progressive miniaturization of hair follicles in selected areas of the scalp (frontal, temporal, and vertex), in genetically predisposed individuals, due to androgens activity such as dihydrotestosterone (DHT).[1] Minoxidil and finasteride, in order to maintain a clinical response, should be done for a lifetime (sometimes they may lose efficacy over the years).[2]

The biological concept of telogen effluvium (TE) was first introduced in 1961 by Klingman, who noted that various events (e.g., toxic, infectious, or metabolic affections) could alter the normal hair cycle, causing sudden and massive hair loss. The trigger event induces the entry of many follicles from the anagen phase (the growth phase) into the telogen phase (the rest phase of hair follicle). This condition usually resolves spontaneously and completely, but it may be a source of anxiety for patients.[3,4] Clinical experience in recent years has suggested the possible existence of different forms of TE related to the type of onset and its clinical course, which can be distinguished into acute and chronic TE. Patients with acute TE complain of conspicuous and sudden hair loss, lasting 2–3 months, which frequently stops spontaneously and is generally followed by complete regrowth. Chronic TE lasts more than 6 months and it usually affects middle-aged women, that describe their hair as thicker than usual before the onset of hair loss.[5] No standardized therapy is available for TE and our approach to this condition is based on ruling

out organic causes, recommending oral supplementation and topical cosmetics with hair-growth properties.[6]

The aim of our study was to evaluate the efficacy, tolerability, and compliance of a treatment with a topical regenerative preparation that mimics autologous PRP, applied once a week in patients affected by TE and mild AGA.

2 | MATERIALS AND METHODS

We enrolled 60 patients, both female and male, aged 18–70 years, suffering from TE and mild AGA. We excluded from the study patients with malignant conditions, or those affected by severe systemic diseases (e.g., diabetes, cirrhosis), patients that were using cosmetic or drug therapies for AGA at least in the 6 months prior to or during the study, patients with inflammatory or autoimmune scalp conditions, pregnant and lactating women, patients with hypersensitivity to one or more components of the product, and patients that needed to check their thyroidal values periodically.

Patients were asked to apply the cosmetic gel, a 15-mL tube of a topical regenerative preparation that mimics autologous PRP, once a week to the scalp with massage. The gel is compounded of aqua butylene glycol, mannitol, *Ascophyllum nodosum* extract, carbomer, cyclodextrin, *Pisum sativum* extract, sodium hydroxide, chlorphenesin, *Halopteris scoparia* extract, disodium EDTA, parfum, sodium dehydroacetate, faex extract, lecithin, tocopherol, ci 19 140, ascorbyl palmitate, citric acid, *Nicotiana benthamiana* hexapeptide-40 sh-polypeptide-76, oligopeptide-1, and oligopeptide-2. The product had to be applied on dry and clean scalp. The study had a duration of 3 months.

The efficacy and the tolerability of the treatment were measured through both qualitative clinical evaluation (by filling out a clinical-anamnestic form) and quantitative evaluation through global photography and trichoscopy. The patient's opinion was considered as well through a self-assessment test, which was performed before and after 3 months of treatment.

2.1 | Clinical evaluation

The clinical evaluation of the outcomes was collected by following this 7-point rating scale of hair loss (−3 = severe worsening, −2 = moderate worsening, −1 = mild worsening, 0 = stability, 1 = slight improvement, 2 = moderate improvement, 3 = major improvement) and it is evaluated by global photography. It consists of a photographic equipment that allows standardized documentation of hair, using overlapping and comparable photos. Each photo is always taken at the same distance, with the patient in the same position, allowing an objective assessment of alopecia progression or improvement.

2.2 | Trichoscopy

Trichoscopy was performed using the Fotofinder® instrument and at the follow-up visit. Both hair quantity and diameter were evaluated in 7-point rating scale of hair quantity and diameter (−3 = severe worsening, −2 = moderate worsening, −1 = mild worsening, 0 = stability, 1 = slight improvement, 2 = moderate increase, 3 = important increase).

2.3 | Patients questionnaire

The patient's evaluation was collected through a questionnaire about their degree of satisfaction (0 not at all satisfied, −1 poorly satisfied, −2 moderately satisfied, −3 definitely satisfied, −4 very satisfied).

In addition, the patient was asked to fill out a questionnaire on the cosmetic tolerability and pleasure of the product at the end of the study.

3 | RESULTS

Sixty patients, including 56 women and four men (mean age was 42 years), with TE and mild-to-moderate AGA were enrolled in the study. Specifically, 20 patients had mild-to-moderate AGA, 18 patients had TE, and 22 patients had TE associated with mild-to-moderate AGA.

Of the 60 patients, 58 fully completed the 3 months of therapy. Two female patients did not complete the study for personal reasons unrelated to treatment. No major side effects were reported by the patients.

3.1 | Clinical evaluation

After 3 months of topical treatment, we rated a mean improvement with a score of 1.88, where a score of 2 represents moderate improvement with cessation of hair loss, while a score of 1 represents a slight improvement with reduction in hair loss.

3.2 | Trichoscopic assessment

The hair quantity of our 60 patients was evaluated through trichoscopy at T0. The mean trichoscopic score was −1.77, where −2 indicates a moderate worsening of hair quantity and −1 a mild worsening of hair quantity. More specifically: 10 were rated −3, 32 patients were rated −2, 12 patients were rated −1, 6 patients were evaluated 0. At the follow-up trichoscopy after 3 months, 58 patients were reassessed. The mean trichoscopic value had risen to +1.51.

The hair diameter of our 60 patients was evaluated as well through trichoscopy at T0. The mean trichoscopic score was −1.47. More specifically: 2 patients were rated −3, 28 patients were rated −2, 26 patients were rated −1, 4 patients were evaluated 0. At the follow-up trichoscopy after 3 months, 58 patients were reassessed. The mean trichoscopic diameter value had increased to +1.37. Results are summarized in Table 1.

3.3 | Patient assessment

After 3 months of treatment, patients gave an average opinion on the efficacy of 2.62. Regarding the cosmetic pleasure of the product (minimum value −2 and maximum value +2) all patients rated between +1 and +2 the product's characteristics, with an average value of +1.31.

All patients tolerated the treatment excellently, with no need to discontinue the treatment. No episodes of itching or erythema were reported.

4 | DISCUSSION

The results of our study show how the gel we used to treat our patients was effective and perceived as pleasant; as a matter of fact, both the clinical and trichoscopic assessment after 3 months displayed a moderate improvement in hair diameter and quantity, while the patient assessment revealed that patients rated the product's characteristics as moderately satisfying (Figures 1A,B and 2A,B). A high compliance to the protocol proves once again how the patients liked and perceived the product as effective. AGA is the most common cause of non-scarring alopecia, affecting up to 50% of women and 80% of men, especially of Caucasian ethnicity, with a frequency increasing with age after puberty.[1] Its pathogenesis shows a pivotal role of androgens in affecting the hair follicle; recently, new studies evidence an adjuvant role of stem cells in the pathogenesis of AGA which leads to the use of therapeutic principles capable of modifying the action of androgens on the hair follicle.[7]

Telogen effluvium is another common cause of non-cicatricial, diffuse hair loss that usually happens after 3 months of a triggering event.[8] In TE, the duration of hair loss can be very variable as it can occur for a few months or up to several years, with no seasonal fluctuation or spontaneous healing. Triggering factors include systemic diseases, stress, drugs, weight loss, iron deficiency, fever, and inflammatory scalp disorders. Hair loss is usually less than 50% of the scalp.[9] Since no standardized therapy is actually available for TE, other than oral supplementation, a topical cosmetic approach with hair-growth properties should be considered.[10,11]

The results of our study showed that a weekly application of a topical regenerative preparation that mimics autologous PRP reduced hair loss in patients with TE, and increased the hair diameter in patients with mild-to-moderate AGA.

This cosmetic stimulates hair follicle stem cells with peptides that mimic the action of endogenous platelet growth factors: they reduce scalp inflammation, stimulate follicular metabolism, and inhibit collagen and elastin catabolism. More specifically, the preparation is rich in plant-derived growth factors that are analogues of EGF, IGF-1, and TGF-beta 2.[12,13] In particular, one of the most important factors is Epitensive™: it contains a plant-derived epidermal growth factor (plant-EGF), a protein that can activate mitosis in the hair follicle and induce the anagen phase in the hair follicle cycle[14];

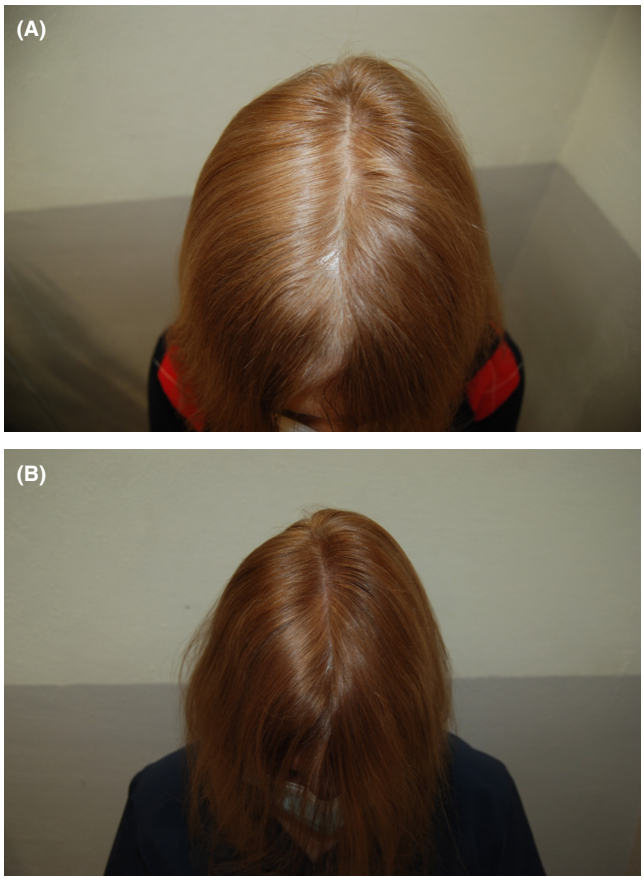

FIGURE 1 Global photography of a patient affected by telogen effluvium and androgenetic alopecia before (A) and after 3 months (B) of treatment.

TABLE 1 Results from the trichoscopic assessment that was done at the beginning of our study and after 3 months.

Trichoscopic assessment	Mean score	Meaning
Hair quantity T0	−1.77	Between moderate and mild worsening of hair quantity
Hair quantity T3	+1.51	Between slight and moderate increase of hair quantity
Hair diameter T0	−1.47	Between moderate and mild worsening of hair diameter
Hair diameter T3	+1.37	Between slight and moderate increase of hair diameter

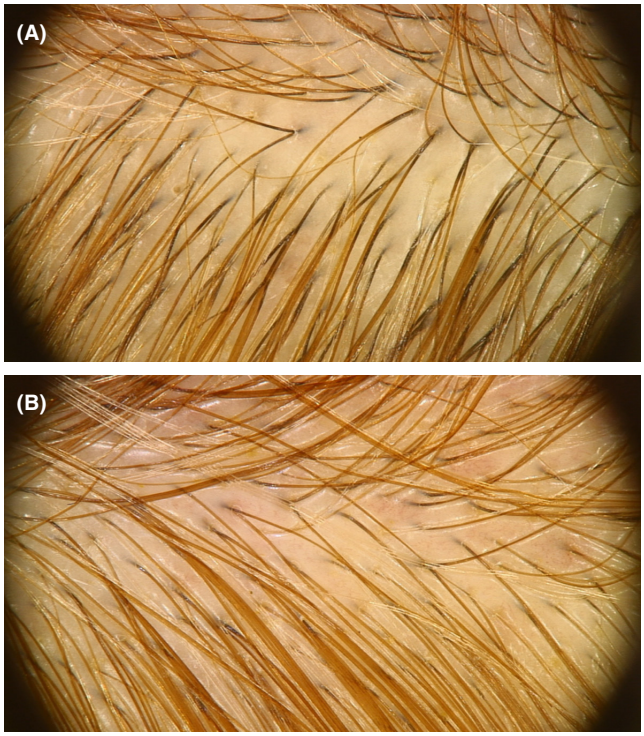

FIGURE 2 Trichoscopy of a patient affected by telogen effluvium and androgenetic alopecia before (A) and after 3 months (B) of treatment.

in combination with Scelleye™, a substance containing plant insulin-like growth factor-1 (plant-IGF-1), it inhibits apoptosis and promotes cell proliferation.[15,16] A combined treatment of IGF-1 and EGF, in vivo, promoted hair regeneration, increased hair follicle density, and induced the expression of anagen phase-related genes.[17] Another active ingredient, Reneseed™, contains plant-derived transforming growth factor beta-2 (plant-TGFβ 2): TGFβ-2 plays a specific role in extracellular matrix synthesis during hair follicle morphogenesis.[18,19]

In addition to growth factors, which are the product's main active ingredients, this preparation contains an extract from brown algae (Actiseane®) with marked anti-inflammatory properties that can reduce IL-6 and IL-1α synthesis, exert antiradical activity in the scalp and protect the hair against UV-induced damage.[20] Finally, this cosmetic has a natural probiotic extract obtained from *Saccharomyces cereviasiae* (Vistacell®) that stimulates the ability of cells to biosynthesize and regenerate ATP in the hair follicle, and a *Pisum sativum* seed extract with anti-elastase and anti-collagenase action. The latter promotes the synthesis of glycosaminoglycans and collagen.

The limitations of our study are linked to the low number of patients: a bigger cohort of people could have shown a more realistic picture of the efficacy of the gel.

5 | CONCLUSION

In conclusion, the results of this study demonstrate the ability of a topical regenerative preparation that mimics autologous PRP to safely and effectively improve hair growth and hair loss in patients with TE and mild AGA.

AUTHOR CONTRIBUTIONS

M. Starace, A. Rossi and B.M. Piraccini performed the research. M. Starace, M. Fortuna and B. M. Piraccini designed the research study. S. Cedirian, G. Caro F. Quadrelli and F. Bruni analyzed the data. S. Cedirian, F. Bruni, and M. Starace wrote the paper. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required since our study was based on the application of a cosmetic product. Patients started treatment only after we got written informed consent.

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REFERENCES

1. Piraccini BM, Alessandrini A. Androgenetic alopecia. *G Ital Dermatol Venereol*. 2014;149(1):15-24.
2. Kanti V, Messenger A, Dobos G, et al. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men – short version. *J Eur Acad Dermatol Venereol*. 2018;32(1):11-22.
3. Kligman AM. Pathologic dynamics of human hair loss. telogen effluvium. *Arch Dermatol*. 1961;83:175.
4. Trueb RM. Diffuse hair loss. In: Blume-Peytavi U, Tosti A, Whiting DA, Trueb R, eds. *Hair growth and disorders*. 1st ed. Springer; 2008:259-272.
5. Asghar F, Shamim N, Farooque U, Sheikh H, Aqeel R. Telogen effluvium: a review of the literature. *Cureus*. 2020;12(5):e8320. doi:10.7759/cureus.8320
6. Sardana K, Sachdeva S. Role of nutritional supplements in selected dermatological disorders: a review. *J Cosmet Dermatol*. 2021;21:85-98.
7. Gentile P, Garcovich S. Advances in regenerative stem cell therapy in androgenic alopecia and hair loss: wnt pathway, growth-factor, and mesenchymal stem cell signaling impact analysis on cell growth and hair follicle development. *Cell*. 2019;8(5):466. doi:10.3390/cells8050466

8. Alessandrini A, Bruni F, Piraccini BM, Starace M. Common causes of hair loss – clinical manifestations, trichoscopy and therapy. *J Eur Acad Dermatol Venereol*. 2021;35(3):629-640. doi:10.1111/jdv.17079
9. Rebora A. Telogen effluvium: a comprehensive review. *Clin Cosmet Investig Dermatol*. 2019;12:583-590.
10. Hughes EC, Saleh D. Telogen effluvium. *StatPearls [Internet]*. StatPearls Publishing; 2022.
11. Alessandrini AM, Bruni F, Piraccini BM, Starace M. The effectiveness and tolerability of preformed growth factors vehiculated through iontophoresis on patients with androgenetic alopecia and telogen effluvium: a clinical study. *Dermatol Pract Concept*. 2021;11(3):e2021082. doi:10.5826/dpc.1103a82
12. Bernard BA. The life of human hair follicle revealed. *Med Sci (Paris)*. 2006;22(2):138-143.
13. Shin H, Yoo HG, Inui S, et al. Induction of transforming growth factor-beta 1 by androgen is mediated by reactive oxygen species in hair follicle dermal papilla cells. *BMB Rep*. 2013;46(9):460-464.
14. Lipotrue. Epitensive Intense Antiaging Plant-EGF. https://www.ulprospector.com/documents/1585037.pdf?bs=34060&b=749009&st=20&r=eu&ind=personalcare
15. Lipotrue. Scelley. https://lipotrue.com/products/scelleye/
16. Botchkareva NV, Ahluwalia G, Shander D. Apoptosis in the hair follicle. *J Invest Dermatol*. 2006;126(2):258-264.
17. Zhao B, Li J, Chen Q, et al. A treatment combination of IGF and EGF promotes hair growth in the angora rabbit. *Genes (Basel)*. 2020;12(1):24.
18. Reneseed the Seed of Youth. https://www.ulprospector.com/documents/1597671.pdf?bs=34060&b=1383039&st=20&r=eu&ind=personalcare
19. Kim H, Choi N, Kim DY, Kim SY, Song SY, Sung JH. TGF-2 and collagen play pivotal roles in the spheroid formation and anti-aging of human dermal papilla cells. *Aging (Albany NY)*. 2021;13(16):19978-19995.
20. Rocha DHA, Pinto DCGA, Silva AMS. Macroalgae specialized metabolites: evidence for their anti-inflammatory health benefits. *Mar Drugs*. 2022;20(12):789. doi:10.3390/md20120789

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