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Re-Densification Effect of Pressure-Injected Peptide-Hyaluronic Acid Combination on Male Androgenic Alopecia

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Abstract

Introduction: Mechanism of male androgenic alopecia (MAGA) is complex and leads to an excessive hair shedding and decreased hair density. Oral, topical, and injectable autologous treatments demonstrate ability to stimulate hair re-growth, but the response is suboptimal or plateaus off. Synthetic combination of the peptide complex and hyaluronic acid (P-HA) demonstrated hair regrowth in alopecia patients. Electronically-operated pneumatic injections (EPI) generate micro-trauma in the dermis and under wound-healing conditions may enhance regeneration effect of P-HA. **Methods:** Subjects seeking improvement of their male pattern hair loss (Hamilton-Norwood type 2 - 4) received the P-HA treatments through EPI. The course included 4 treatments every two weeks over the 8-week period. In 6 months, the hair growth was assessed comparative to baseline by global clinical photography and digital phototrichograms. The treatment safety and tolerability were documented through the whole study period. **Results:** Twelve men (30 - 45 years old) completed the treatment course with high tolerability and without adverse events. Post-treatment assessment of the previously bald areas showed improved coverage on the clinical photographs. The phototrichograms demonstrated statistically significant increase in terminal hair density by 36%, cumulative hair thickness by 37%, and follicular units by 20%; all contributing to a 38% increase in cumulated hair density (all $p < 0.05$). **Conclusion:** Electronic pneumatic injections are well tolerated and can be safely used for the needle-free administration of the peptide-hyaluronic acid combination in MAGA therapy. We achieved significant hair re-densification in the balding scalp. The exact role of the EPI-induced impact in the hair re-growth mechanism remains to be ascertained.

Keywords

Jet Injections, Electronic Pneumatic Injections, Male Androgenic Alopecia,

Bioactive Peptides, EnerJet

1. Introduction

The pathological mechanism of the progressive male-pattern hair loss (male androgenic alopecia, MAGA) is complex and has been linked to hormonal dysfunction, genetic predisposition, exposure to environmental factors, and response to psychogenic stress [1]. The major factor of MAGA pathogenesis is thought to be the undesirable conversion of testosterone to dihydrotestosterone (DHT) under the enzyme 5-α-reductase. Still, contemporary theories propose some other mechanisms [2] including:

- inhibition of Wnt/β-catenin pathway involved in hair follicle (HF) development, hair cycling and hair growth,
- follicular microinflammation in the peri-infundibular region of HF potentially leading to perifollicular fibrosis and even physical blocking of the hair canal [3],
- increased level of prostaglandin PGD2 related to miniaturization of HFs,
- damaging effect of free radicals resulting from the oxidative stress of UV light or smoking.

The pathological changes are expressed in an altered hair cycle, depleted dermal papilla's cells, miniaturized hair follicles, and reduced hair fiber resulting in excessive hair shedding [1] [4].

It has been also postulated that MAGA involves the pathologic depletion of extracellular matrix (ECM) in the follicular bed [5]. The structures and components of ECM (proteins and glycosaminoglycans) provide mechanical and structural support for HFs and give anchorage to the hair shafts [2] [6]. ECM structural proteins (collagens I, III, and VII) are thought to regulate the number of cells re-entering the dermal papilla (DP) during normal hair cycle, thus maintaining the size of hair follicle [7]. It is assumed that under androgenic dysfunction, gradually decreasing levels of ECM proteins in the follicular bed contribute to progressive miniaturization of hair follicles and loss of hair support and anchoring [4] [6]. Thus, promotion and replenishment of ECM components seems to be the path to maintaining HF size and diminishing hair shedding.

Conventional therapy includes FDA-approved oral finasteride and topical minoxidil, or emerging injectable autologous therapy (platelet-rich plasma or adipose derived stem cells). Although they demonstrate the ability to reduce hair loss and stimulate hair re-growth, the response is selective, suboptimal or plateaus off [2].

Bioactive peptides

As an emerging alternative to conventional therapy, synthetized peptides with therapy-specific bioactivity have been lately introduced to cosmetics, therapeutics, and immunology. Bioactive peptides or biopeptides (BPs) are synthetic

compounds consisting of various amino acid sequences and act as signal transmitters, carriers, or more specific, mimic natural or recombinant growth factors [8] [9]. The molecules are formulated to be stable, compatible with other components, not to exhibit toxicity and be delivered effectively to the skin. BPs demonstrated the ability to suppress proliferation and induce apoptosis of cancer cells *in-vitro* [10], recognize and trap bacteria *in vivo* [11], but clinically they have been implemented mainly for anti-aging therapy [12].

In human HFs, BPs have been shown to have regenerative effects on the microvascular endothelial cells and dermal papilla cells [13]. Nam [14] revealed suppressed apoptosis of DHT-treated human dermal papilla cells by applying a synthesized AC2 peptide. In the study of female telogen effluvium, using a lotion containing peptide combination (decapeptide-18, oligopeptide-54, decapeptide-10, octapeptide-2, decapeptide-19, oligopeptide-71, and decapeptide-28) Kubanov [15] demonstrated a statistically significant decrease in the proportion of telogen hairs and a statistical increase in the proportion of anagen hairs. Rinaldi [16] showed hair re-growth in alopecia patches injected with BP mimicking autologous platelet-rich plasma (octapeptide-2, decapeptide-3, copper tripeptide-1, and oligopeptide-20). Loing [7] achieved a 13% increase of anagen hair density in the group treated with bioactive tetrapeptide-3 combined with *Trifolium pratense* flower extract. The effect was speculated to be due to inhibition of 5-α-reductase activity, reduction of inflammatory reactions, and stimulation of ECM protein synthesis in the vicinity of the hair follicle.

Peptide-HA combination (P-HA)

The polymer implemented in this trial (DR.CYJ Hair Filler, Caregen, South Korea) contains an injectable combination of hyaluronic acid (HA) and a patented formula of 7 peptides: octapeptide-2, decapeptide-10, octapeptide-11, decapeptide-18, decapeptide-28, oligopeptide-54, and oligopeptide-71. The peptide complex is described as acting on hair shaft, follicular bulb, dermal papilla cells and dermal microcapillaries through multifunctional mechanism [17]:

- Octapeptide-2 promotes hair growth by activating HF stem cells and enhancing migration and proliferation of keratinocyte contributing to *de novo* HF growth [18].
- Decapeptide-10 stimulates angiogenesis and microcirculation for improving vascularization of the treated scalp and nourishment to the hair shaft.
- Octapeptide-11 inhibits hair cell apoptosis caused by oxidative stress of UV exposure, smoking, or other environmental factors.
- Decapeptide-18 induces formation of hair placodes and generates new hair follicles by β-catenin and the shh signal.
- Decapeptide-28 inhibits hair loss by acting on the signaling pathways of the stem cells in the follicular matrix toward activation of the growth anagen phase and delay of the transitional catagen phase.
- Oligopeptide-54 inhibits hair loss by down-regulation of pathogenic mediators DKK-1 and BMP4, which prematurely initiate catagen phase and inhibit activation of HF stem/progenitor cells during anagen phase [19] [20].

- Oligopeptide-71 promotes hair re-growth by activating the Wnt/β-catenin signaling pathway towards HF growth and proliferation of DP cells [21].

HA forms ionic bonds with the peptide complex and, once penetrated in the skin, slowly releases the oligopeptide material within a 2-week period. Additionally, HA induces skin hydration and improves the metabolism of follicular fibroblasts.

The product is an injectable medical device Class III and has a CE marking (CE 2265). It is indicated for the treatment of male and female patients suffering from the non-scarred alopecia or for increase in survival of the transplant in hair transplantation surgery. As to date, information on the clinical efficacy of DR. CYJ Hair Filler for hair re-growth is limited. The case series presented on the product website (http://www.drcyjhairfiller.com/) demonstrates increase in hair density (HD) and hair thickness (ranges 12.3% - 36.4% and 8.8% - 26%, respectively) after the treatment course of 4 treatments over the 8-week period. The drug was injected in a series of intradermal injections lined over the targeted scalp every 0.2 - 0.3 cm horizontally and every 1 cm vertically. At each point, 0.02 - 0.05 ml of the drug was injected. In order to alleviate painful injections into the scalp, the manufacturer recommends using topical anesthetic cream [drcyjhairfiller.com].

Electronic pneumatic injections (EPIs)

In the current study, we alternated the standard administration method by using needle-free electronically controlled pneumatic injections, also known as jet injection. EPI is recognized as a beneficial and safe route for administration of dermal fillers in the treatment of facial wrinkles, skin laxity, and scars. The treatments have been shown to provide minimal discomfort for the patients. Indeed, the potential side effects of EPI technology include skin bruises, edema, itching and localized pain [22] [23] [24].

EPI technology is based on the principle of a liquid jet, or pressurized stream of fluid, pneumatically ejected from the injection device under electronically-controlled settings which provide uniformity for injection volume and pressure. The stream penetrates the skin through a minuscule entry point of approximately 200 microns and undergoes omni-directional dispersion reaching the upper, mid, or deep dermis. Dispersed micro-droplets traumatize surrounding tissues at microscopic level and initiate a wound healing cascade toward neocollagenesis and skin regeneration [25]. Micro-trauma is not accompanied with inflammation or significant damage to the tissue or blood vessels [26] [27].

The advantages of electronic pneumatic jet injections include the ease of administration and the ability to uniformly maintain dose and depth of injection independent of the injector's skills and experience [28] [29]. Software of the advanced EPI device controls the depth of drug deposition which can be adjusted from papillary and reticular dermis to subcutaneous fat.

Previously, we implemented EPIs for correction of rhytidosis in the aged skin by administration of cross-linked HA [23]. Efficacy assessed after 3 months by objective 3D imaging demonstrated statistically significant reduction in wrinkle

depth (22.6%) and wrinkle volume (17.4%) and a 20%-increase in skin elasticity. The dermis height measured by skin sonography revealed a mean increase by 20%. EPI treatments provided minimal discomfort and high acceptance among the treated patients. We speculated the improvement was related to the synergy between HA's and micro-trauma's regeneration mechanisms. It was hypothesized that this effect could be extrapolated to stimulate hair growth.

2. Materials and Methods

We conducted a prospective pilot study with the objective to explore the safety and efficacy of an EPI-injected P-HA combination to reverse the pathological conditions of MAGA. This study was performed in accordance with the 1975 Declaration of Helsinki and its later amendments.

Patient selection

Twelve subjects seeking improvement of their male pattern hair loss in the hair restoration clinic (Clinica Elite Laser, Madrid, Spain) and hair transplant clinic (Clinica MC360, Madrid, Spain) voluntarily agreed to receive the jet-injected treatment with the P-HA combination. All subjects signed an Informed Consent in which they declared to be aware of the treatment method and allowed the use of photographic records for scientific publications. Subjects with cardio-vascular diseases, diabetes, cancer, coagulopathies, or receiving immunosuppressive drugs or steroids or pharmaceutical treatment for hair loss were excluded. Subjects with skin infection in the area intended for treatment were also disqualified. All approved patients had not taken oral finasteride or and topical minoxidil treatments for at least 12 months prior to the P-HA injections, and they were advised to maintain abstinence. Detailed history with respect to duration of hair loss and preexisting medical conditions was recorded. After the baseline clinical examination, each participant received 4 treatments every two weeks over the 8-week period. In 6 months after completing the treatments, participants returned to the clinic for the follow-up assessment of hair growth.

Injection procedure

At each treatment, the drug was administered in a series of intradermal injections performed by the jet-injection device (EnerJet2.0, PerfAction Technologies, Israel). The device software allows for a controlled adjustment of the injection pressure in the range of 2 - 6 bars and the injection volume in the range of 0.05 - 0.15 ml. After cleansing with 2% chlorhexidine gluconate in 70% (v/v) isopropyl alcohol, P-HA was administered to designated areas of hair loss (frontal and anterior mid scalp) in multiple needle-free pneumatic injections. Our previous experience demonstrated minimal discomfort of EPIs [23], therefore no local anesthesia was implemented for current treatments either.

The manufacturer's injection strategy was modified in order to implement specifics of the jet injection technology. To benefit from the wide intradermal dispersion achieved with EPI's [27] [28], the injection points were spread every 1 cm *vs.* manufacturer's 0.2 - 0.3 cm (**Figure 1**).

The single injection volume of 0.07 ml exceeded manufacturers recommended 0.05 ml in order to substitute the loss associated with retrograde back flow from the injection entry point. Injection pressure was adjusted within the range of 2.5 - 3.0 bars in order to achieve the optimal skin papule, the end-point of dermal penetration (Figure 2).

Efficacy and safety assessment

The baseline clinical examination included global clinical photography, digital phototrichograms and grading of the hair loss according to Norwood–Hamilton scale, from type I (no baldness) to type VII (severe baldness).

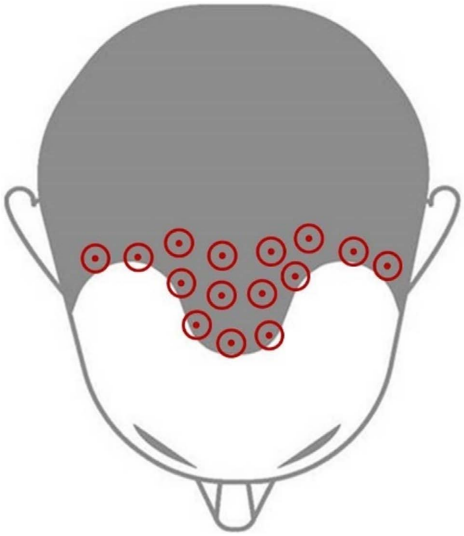

Figure 1. EPI treatment scheme: injection points are spread in 1-cm grid over the alopecic region.

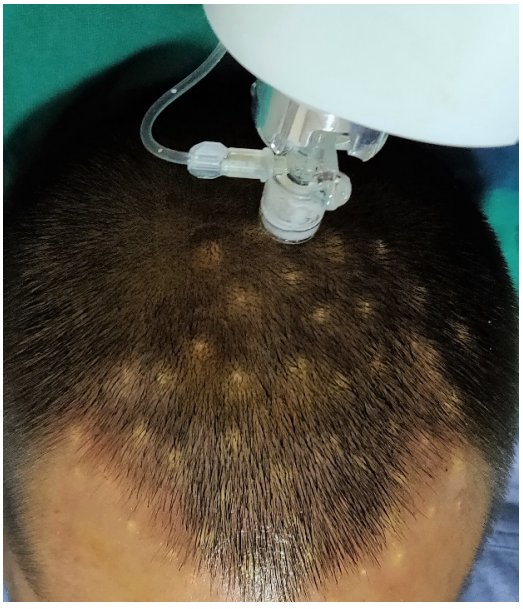

Figure 2. Dermal papules appearing after the pneumatic injections indicate skin penetration and intradermal spread of the drug. The papules spontaneously resolved within a few hours.

For each patient, the phototrichogram was performed on the 2 cm-diameter spot alone the mid-line in the frontal region indicated for the treatment. The spot was shaved to ensure adequate trichogram measurements and was marked by a semi-permanent tattoo to be evaluated after the treatment. Digital phototrichogram images were taken at 20×-magnifications using the digital Medicam® 1000 system (FotoFinder Systems GmbH, Germany) and stored on a linked computer. The system and accompanied software (SW) (Trichoscale Pro, FotoFinder Systems GmbH, Germany) allows quantification and analysis of the diffused hair loss. The software is validated for MAGA [30] and automatically calculates number of hairs, mean HD (hairs/cm^2), terminal and vellus hair percentage, hair thickness, and number and density of follicular units – all within a standard 0.903 cm^2 area (1.07 cm diameter area). During SW evaluation, all hairs with thickness > 40.0 μm are described as terminal hairs, while hairs with lesser thickness are described as vellus hairs.

Efficacy in hair growth was assessed at the patient's visit 6 months after the last treatment. The assessment included repeated global clinical photography and the quantitative phototrichogram performed by the same phototrichogram device on the same demarcated point. Post-treatment images and trichogram measures (number of hairs, hair density, vellus and terminal hair density, cumulated hair thickness, number and density of follicular units) were analyzed in comparison to the baseline. Statistical analysis of the trichogram parameters before and after the treatment was automatically performed by the Trichoscale Pro SW. The Student t-test was used in order to obtain the results mean values and calculate p-value (<0.05). The primary end-point was comparative improvement of hair density and number of hairs in the treated frontal region.

Safety was assessed by recording adverse events at the treatments and the follow-up visit. Additionally, patients rated the treatment discomfort on the (0 - 10) Numeric Pain Rating Scale (NPRS) at each treatment.

3. Results

Twelve men (range 30 - 45 years old) with self-perceived thinning and recessing hair in the scalp within last 12 months were enrolled in the trial. The receding hairline was presented in the frontal and temporal scalp and correlated with Hamilton-Norwood type 2 - 4. No skin alterations (flaking or calcification) were observed in the scalp skin.

All of the participants completed the treatment course and were available for the follow-up assessment 6 months thereafter. No significant adverse events were documented at the treatment procedures or during the follow-up period. At the follow-up visit, all participants reported appreciable coverage in the previously bald areas which was consistent with investigator-evaluated improvement in the clinical photographs (**Figure 3**).

Comparative analysis by the Trichoscale Pro software demonstrated a statistically significant increased number of hairs and follicular units along with en-

hanced cumulative hair thickness ($p < 0.05$) (Table 1).

Mean total HD increased by 45 ± 3 hair/cm^2 ($p < 0.05$) or 38%, compared to pre-treatment values. Although the growth was observed in both terminal and vellus quantities, the density of terminal hairs rose at a higher rate, which is indicative for post-treatment reversal in hair loss. Number of hairs in anagen phase increased which indicated activation of hair growth; however anagen/telogen ratio was not investigated in our study (Figure 4).

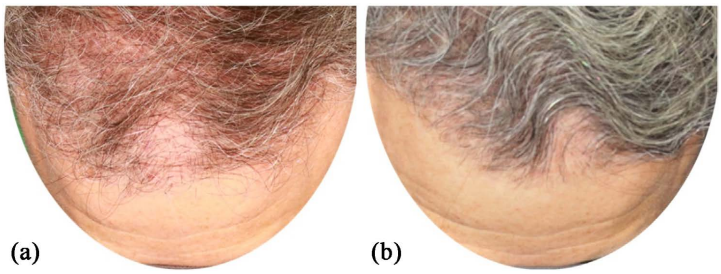

Figure 3. Clinical photographs of a 45-yearl old male patient with Hamilton-Norwood type III androgenetic alopecia: at baseline (a) and 6 months after the treatment (b).

Table 1. Trichoscale analysis of relevant hair parameters at baseline and 6 months after the treatment (average ± standard deviation).

	Baseline	After treatment	Dynamics of change (%)
Number of hairs, per 0.903 cm^2	107.2 ± 15.3	148.0 ± 19.9	38
Hair density, per cm^2	118.6 ± 17.0	163.8 ± 22.0	38
Vellus hair density, per cm^2	15.4 ± 8.6	19.5 ± 14.0	26
Terminal hair density, per cm^2	93.8 ± 16.1	127.2 ± 20.1	36
Cumulated hair thickness, mm/cm^2	7.1 ± 1.2	9.7 ± 1.7	37
Number of follicular units, per 0.903 cm^2	76.5 ± 8.3	91.7 ± 9.8	20
Follicular units' density, per cm^2	107.2 ± 15.3	148.0 ± 19.9	20

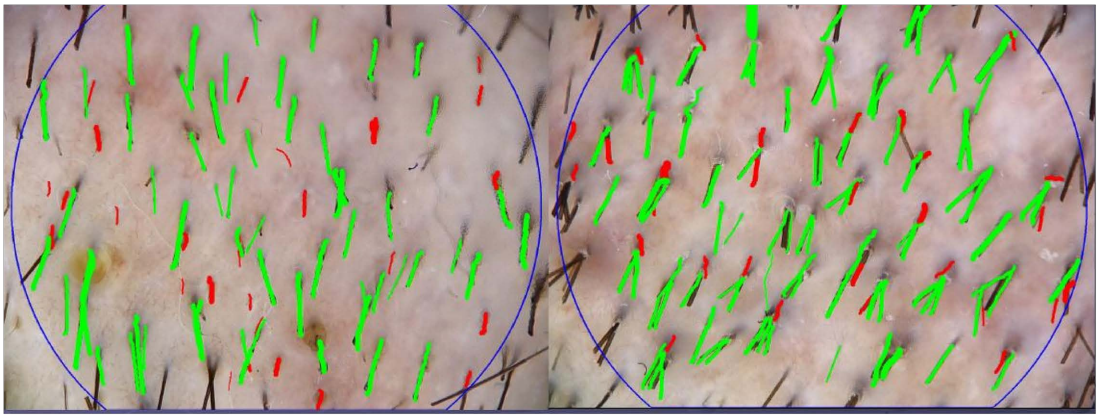

Figure 4. Trichoscopic images at baseline and 6 months after the treatment: telogen hair strands coded as red and anagen hair strands coded as green.

4. Discussion

Although the exact role of DHT in the male alopecia remains to be defined, it is postulated to be associated with pathological changes in the hair cycle and miniaturization of both hair and follicular unit [1]. Shortening of the growth anagen phase and premature entry into resting catagen phase enhances apoptosis of hair cells [7] [31]. In addition, degeneration of ECM results in fewer DP cells re-entering the dermal papilla that reduces the size of a hair follicle [4]. The large terminal hairs became replaced by small vellus hairs that cause excessive shedding and decrease in hair density [31].

Non-surgical management of MAGA

The current pharmacological management of MAGA is limited to oral finasteride and topical minoxidil lotion. Finasteride is a 5α-reductase inhibitor, which prevents the conversion of testosterone to DHT. Finasteride treatment averts further hair loss but has been linked to anxiety, depression, and erectile dysfunction. Treatment cessation is connected with resumption of hair loss [32]. Minoxidil is a vasodilator with the potassium channel blocking mechanism and promotes vascularization via synthesis of vascular endothelial growth factor (VEGF) in dermal papilla. Generally safe, the treatment requires prolonged time to achieve clinical effect, and is associated with a large percentage of non-responders [33]. Being effective for MAGA patients, both drugs need to be administered daily which creates dependence for the patients.

Recently, various injectable drugs demonstrated potential for MAGA management. Subcutaneous injections of finasteride-loaded microspheres revealed efficacy in animal models [34] but lack proof in human subjects. Injections of botulinum toxin were postulated to reduce vasculature pressure and increase transcutaneous pO_2 with clinical improvement demonstrated on photographic assessment [35].

In contrast to finasteride and minoxidil, therapeutic options based on autologous sources have been studied in the last decade. Platelet-rich plasma (PRP) and micrografts containing mesenchymal stem cells from hair follicles and adipose tissue have demonstrated hair regrowth in patients with androgenetic alopecia. Injection of PRP containing growth factors has been shown to improve hair count, hair thickness and hair density [30] [36]. The plasma is believed to promote hair differentiation and inhibit apoptosis of HF cells. Scalp injection of the suspension containing micrografts enriched with human hair follicle mesenchymal stem cells (HFSCs) or human dermal adipose tissue-derived HF stem cells (ADSCs) has been shown to exert clinical and trichoscopic effects in the patients affected by MAGA [37] [38]. HFSCs derived from the dermal papilla or dermal sheath of the human HF are believed to activate proliferation of the progenitor cells in hair follicles. In their turn, ADSCs secrete several growth factors (hepatocyte growth factor (HGF), VEGF, insulin - like growth factor (IGF), and platelet-derived growth factor) inducing HF size during hair development [39] [40]. Despite the fact that this therapy has being accepted, the procedures are

time-consuming and still bear cost associated with preparation of the injectable autologous material. In addition, the preparation methods, dose and administration protocols are not yet standardized, and the regenerative mechanism is still being studied.

Biopeptides in the management of MAGA

Biopeptides are seen as an emerging cosmeceutical therapeutic modality for MAGA. The mechanisms of action vary based on the oligopeptides contained. In the current study, we investigated the effect of a patented peptide-HA combination on hair growth in male patients with androgenic alopecia. The study participants received a series of 4 treatments with the delivery method modified from traditional needle injections to the electronically-controlled pneumatic needle-free injections. This novel delivery method is believed to enhance the therapeutic effect of P-HA through the healing mechanism of the micro-trauma which induces the regeneration of ECM components [25] [26]. The participants were re-evaluated in 6 months after receiving the last treatment and the data was assessed from efficacy and safety point of view. Pre- and post-treatment dermoscopy images of the treated regions were compared and analyzed by the Trichoscale Pro SW. Analysis demonstrated statistically significant increase ($p < 0.05$) of the terminal HD by 36%, cumulative hair thickness by 37%, and follicular units by 20%; all contributing to a mean 38% increase in overall HD, the main indicator of hair loss in MAGA.

Achieved improvement in hair density is close to that shown in autologous therapy studies. Gkini [41] demonstrated a 9.19% HD increase at 6 months after the PRP treatment. Gentile [36] compared activated and non-activated PRP and reported augmented HD for both (28 ± 2 hair/cm^2 and 15 ± 3 hair/cm^2, respectively). In another comparative study by Gentile [37], a 29% HD increase was achieved in the scalp treated with HFSC *vs.* to a 1% with placebo. Anderi [42] demonstrated a 36% growth in HD at 6 months after injecting autologous ADSCs into the scalp of patient with alopecia areata.

Pressure jet mechanism of action

The role of the pressure-injected jet on the hair regrowth mechanism is possibly similar to its action in the repair of aging skin. Physical tension applied by the micro-droplets on the surrounding extracellular matrix results in the morphological stretching of fibroblasts and micro-injury to the encountered collagen fibers [43]. The subsequent healing mechanism stimulates collagen synthesis without inflammation or excessive scarring [44].

Based on our own experience with EPI-delivered HA fillers [23], we feel that the results achieved in this study to be related not only to the P-HA mechanism, but also to the jet-generated micro-trauma which appears to enhance the treatment output by stimulating ECM components in the follicular bed. The pressurized jet stream provides propulsion of the drug solution into skin where it absorbed in the epithelium of hair follicles, as demonstrated by high-resolution confocal microscopy [45]. The spread of the drug micro-droplets applies tension on the extracellular matrix causing sub-clinical micro-injury and stimulating

collagen synthesis resulting in a long-term beneficial effect [25] [45]. The mechanical effect of the jet-infiltrated solutions activates a latent form of transforming growth factor (TGF-β) and induces the proliferation of fibroblasts toward the synthesis of type I collagen [44]. In addition, we hypothesize that the forced dispersion of the micro-droplets by the pressure induced jet may result in hair regeneration through mechanical stretching [46]. As demonstrated by Chu [47], the stretch induces activation of M2 macrophages and upregulation of growth factors (HGF and IGF-1), functional mediators in hair regeneration.

An additional effect is thought to come from the HA component of the P-HA polymer. Aside from the biophysical stimulation of dermal fibroblasts, jet-injected exogenous HA has been shown to enhance structural integrity of the ECM and provide tissue repair through interactions with cell surface receptors [48] [49].

Precise control of the drug deposition appears to be highly beneficial in MAGA treatments and targets the HF itself [50]. Topically applied minoxidil has limited performance in part due to restraints in bypassing the stratum corneatum barrier. Nano agents designed for drug delivery through the hair appendage ducts (trans-appendageal pathway) still lack implementation in clinical practice [51]. In contrast, materials delivered by EPI easily penetrate the epidermis and are precisely deposited at the operator-targeted depth [27] [52]. In the current trial, the drug was injected at 2 - 2.5 bar pressure in order to reach the superficial dermis. With the average 6-mm lateral distribution of the drug [45], we were able to affect multiple hair follicles in the vicinity of one jet entry point, compared to a traditional needle injection.

Tolerability and safety

Fear of needles (trypanophobia) also posts an obstacle for alopecia management [53]. Needle injections into the scalp are painful and barely tolerated by patients. Needle-free EPIs, however, are known to provide minimal discomfort. The high-speed jet stream delivers rapid penetration into the skin at the lowest sensitivity [22] [23] [29]. That makes the treatments easily tolerable to maintain patient's adherence and guarantee its outcome [54] [55]. Although we did not purposely select the patients with known trypanophobia, the treatment compliance was maintained through the trial and all patients finished the treatment course. EPIs were performed without any anesthetics, contrary to the manufacturer's recommendations for additional analgesia. Injection pain was documented at the average 2.4 of NPRS score and rated as minor discomfort.

No major adverse events requiring medical attention were observed thus the treatments were considered safe. Small bleeding from the injection point was a common occurrence caused by the jet propagation through the capillary plexus in the superficial dermis. It was easily controlled by applying direct pressure and did not slow the injection sequence. The histological studies [22] demonstrated that the jet is not powerful enough to cause damage to the skin anatomical structures such as skin appendages (hair follicles, sebaceous glands and sweat glands) or dermal vasculature. We did not observe any signs of scarring at the

injection points on the magnified trichoscopy images 6 months after the treatment.

Limitations

To our knowledge this is the first clinical study for which MAGA therapy was implemented through EPIs. For hair growth, EPIs are limited to the administration of steroids into alopecia areata lesions [56] [57] [58]. Although the achieved hair re-growth was in-line with the published results, the trial is limited by the small population, short follow-up period, and lack of control group. We were not able to conclude whether the hair growth was solely due to P-HA or to the synergy with EPI mechanism. The mechanism and longevity of the hair growth effect remains to be explored.

5. Conclusion

We demonstrated that electronically controlled pneumatic injection can be well tolerated and safely used for the needle-free administration of the peptide-hyaluronic acid combination in MAGA therapy. With minor modifications of the manufacturer's treatment protocol, we achieved significant hair re-densification in the balding scalp. The exact role of the EPI-induced impact in the hair re-growth mechanism remains to be ascertained.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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