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Comparative study of the effectiveness of intradermotherapy associated or not with microneedling and topical solution in reducing hair loss in men with androgenetic alopecia

Estudo comparativo da eficácia de intradermoterapia associada ou não a microagulhamento e solução tópica na redução da perda capilar em homens com alopecia androgenética

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ABSTRACT

Introduction: Androgenetic alopecia impacts patients psychologically. Androgenetic alopecia is an androgen-dependent condition characterized by hair follicles miniaturization, shortened anagen phase, and prolonged telogen phase. The increasing search for hair therapies to improve this condition leads to the need for robust methods to compare the effectiveness of treatments, such as standardized photographs and clinical evaluation.

Objective: This study comparatively assessed the efficacy of intradermotherapy associated or not with microneedling and application of sterile topical solution whose active components are Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract, and Silanediol salicylate.

Methods: Standardized photographs and patients' clinical findings were compared per experimental group in a blind and paired manner by dermatologists, with attribution of scores referring to hair loss improvement.

Results: The group treated with the therapeutic association obtained better results than the group treated with intradermotherapy alone (control), with 70% of patients showing improvement scores against 54%. There was a statistically significant difference between the treatment groups.

Conclusion: The therapeutic association of intradermotherapy with microneedling followed by topic treatment was significantly more effective in improving male hair loss compared to control.

Keywords: Alopecia; Photography; Hair preparations

RESUMO

Introduction: *a alopecia androgenética impacta psicologicamente os pacientes acometidos. A alopecia androgenética é uma condição andrógeno-dependente caracterizada pela miniaturização dos folículos, com encurtamento da fase anágena e aumento da fase telógena. A busca cada vez maior por terapias capilares para melhorar esse quadro leva à necessidade de métodos robustos para comparar a eficácia de tratamentos, como as fotografias padronizadas e a avaliação clínica.*

Objetivo: *neste estudo, avaliou-se comparativamente a eficácia da intradermoterapia associada ou não a microagulhamento e aplicação de solução tópica estéril cujos componentes ativos são Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract e Silanediol salicylate.*

Métodos: *fotografias padronizadas e achados clínicos dos pacientes de cada grupo experimental foram comparados de forma cega e pareados por avaliadores dermatologistas, com atribuição de escores referentes à melhora do quadro de perda capilar.*

Resultados: *o grupo tratado com a associação terapêutica obteve resultados melhores em relação àquele tratado somente com intradermoterapia (controle), com 70% dos pacientes apresentando escores de melhora contra 54%. Houve diferença estatisticamente significativa entre os grupos de tratamento.*

Conclusão: *a associação terapêutica entre intradermoterapia e microagulhamento com aplicação de solução tópica foi significativamente mais eficaz na melhora da perda capilar masculina comparada ao controle.*

Palavras-chave: *Alopecia; Fotografia; Preparações para cabelo*

Original Article

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INTRODUCTION AND OBJECTIVE

Androgenetic alopecia is a condition that psychologically and emotionally impacts patients, affecting self-esteem, self-confidence, and image perception of each individual and significantly influencing their quality of life.

In men, androgenetic alopecia and telogen effluvium are among the most common causes of hair loss. Androgenetic alopecia is an androgen-dependent condition characterized by the miniaturization of follicles, with a shortening of the anagen phase and an increase of the telogen phase in the hair development cycle.[1-3]

The pharmaceutical industry has been increasingly searching for the development of new hair therapies to treat patients suffering from hair loss, which makes research and methodologies necessary to compare these therapies to offer greater efficacy in the patients' treatment.

Several methods can be used to diagnose hair growth cycle abnormalities and to evaluate the treatment's effectiveness. Among these, we can highlight the dermatological clinical evaluation in the office and the standardized photo.[4]

The standardized photo corresponds to the capture of images of the patients under controlled and standardized conditions and their subsequent comparison before and after treatment to verify the improvement in hair growth.[5]

This research compared standardized photos and data from the medical records of 20 men with advanced baldness treated at a private dermatological hair restoration clinic in São Paulo, Brazil, to determine which treatment was more effective. Of these, half were treated with intradermotherapy, and half received intradermotherapy associated with microneedling and application of a sterile topical solution, whose active components are Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract, and Silanediol salicylate.

METHODS

Study design: We conducted a unicentric retrospective comparative study between two groups of patients submitted to different treatment protocols for hair loss. The evaluating dermatologists received the information to assess the patients in each group blindly, thus avoiding any bias.

Procedures for selection of patients and evaluators:

We selected medical records and standardized photos of 20 men with advanced baldness previously treated at a private dermatological hair restoration clinic in São Paulo, Brazil.

Among the 20 selected participants, we elected the medical records of 10 patients who received intradermotherapy treatment (three sessions) and 10 patients who received intradermotherapy treatment (three sessions) associated with microneedling and application of a sterile topical solution with active components Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract, and Silanediol salicylate. The treatment time for each patient was five months between the first and the last session. The sessions were distributed as follows:

- Session 1: held on the date of the patient's surgery;
- Session 2: performed two to three months after surgery;
- Session 3: conducted four to five months after surgery.

The inclusion criteria for the selection of participants were: (1) men who were treated at the clinic; (2) patients with advanced degree of baldness, that is, with Hamilton-Norwood pattern androgenetic alopecia grade ≥5, with vertex involvement and insufficient donor area for hair transplantation to treat the region; (3) patients without existing comorbidities; (4) patients who had not undergone previous drug delivery treatment at the site for at least three months before the hair transplant; (5) patients treated at the clinic with one of the following therapies: intradermotherapy or intradermotherapy associated with microneedling and application of an ampoule containing a sterile topical solution with Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract, and Silanediol salicylate.

The exclusion criteria were: (1) women; (2) patients with Hamilton-Norwood pattern androgenetic alopecia grade <5; (3) patients who had undergone previous drug delivery treatment at the site for less than three months; (4) patients with telogen effluvium due to other causes, evaluated in the initial consultation through clinical exams (zinc, copper, ferritin, total proteins, and fractions, T3, T4, TSH, vitamin B12 dosage, free and total testosterone, ANA-HEp-2, TRAB, rheumatoid factor).

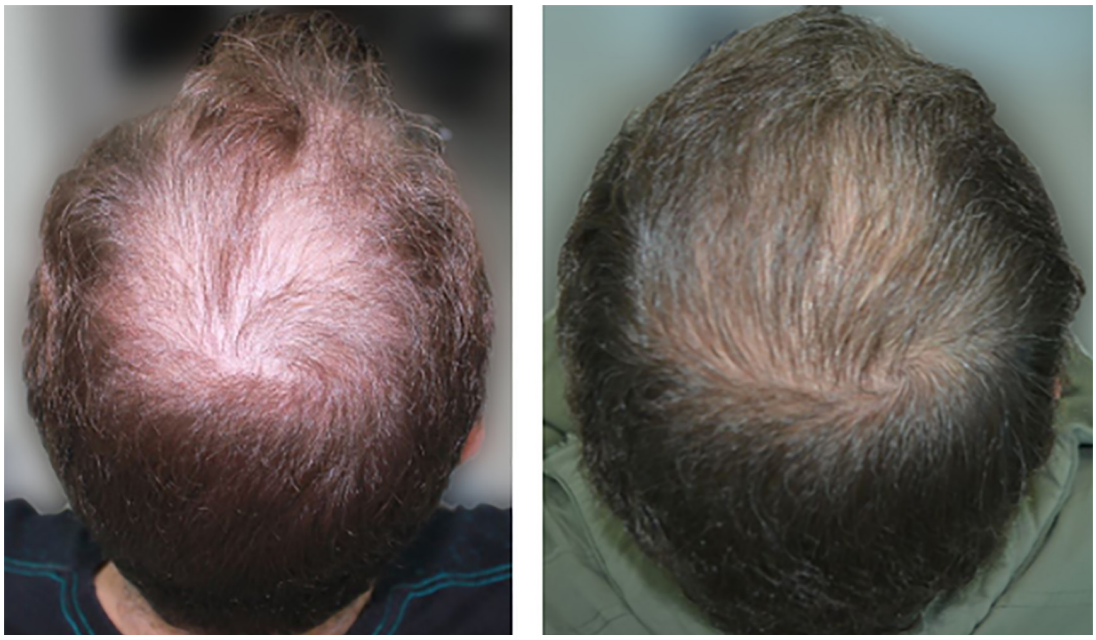
We selected five dermatologist evaluators to blindly assess the medical records and standardized photos of patients in each experimental group. The inclusion criteria for the selection of evaluators were: (1) dermatologists who are members of the Brazilian Society of Dermatology; and (2) with knowledge of trichology and hair loss assessment. Exclusion criteria were: (1) physicians from other specialties and/or non-members of the Brazilian Society of Dermatology; (2) professionals not trained and not able to assess hair loss; and (3) the principal investigator of the study.

PROCEDURES

We selected the medical records and standardized photos of 20 men with advanced baldness before and after hair treatment from the Research Institution's database to verify clinical findings and subsequent comparison. The standardized photos were obtained according to the example in figure 1.

Of the 20 patients, 10 underwent treatment with intradermotherapy (Group 1), and 10 received intradermotherapy combined with microneedling and application of a sterile topical solution with the active components Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract, and Silanediol salicylate (Group 2). The details of the treatment procedures are:

- Group 1: at each session, only intradermotherapy was administered.



INITIAL POST-TREATMENT CONSULTATION

Figura 1: Standardized photos of patients

- Group 2: at each session, intradermotherapy was initially administered, followed by microneedling using a roller with a needle depth of 1.5 mm. The endpoint was pinpoint bleeding. Microneedling aimed to open microchannels in the skin to allow the investigational product to work. After microneedling, 1 mL of a sterile topical solution composed of Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract, and Silanediol salicylate was applied to the experimental region. The topical solution was injected by dripping over the area using a disposable syringe, followed by a gentle massage. After application, patients were properly instructed to keep the active in contact with the skin for four to six hours.

After selecting the patients, five evaluators (dermatologists) received the compiled data to assess comparatively before and after treatment to assign scores referring to the perception of improvement in hair loss.

For this purpose, the evaluators received, blindly and randomly, the images of the 20 patients before and after treatment, in a paired way, and assigned a score referring to the improvement of the hair loss condition:

-3 = significant worsening of the condition; -2 = worsening of the condition; -1 = mild worsening in the condition; 0 = no difference after treatment; 1 = mild improvement in the condition; 2 = improvement in the condition; 3 = significant improvement in the condition.

Method of results evaluation:

The scores of the patients in each group were submitted to frequency analysis to determine the percentage of scores indicating improvement or non-improvement of the condition per treatment. Based on the frequencies, we verified which treatment presented the greatest number of patients with significant improvement.

Also, the 7-point scale scores were compared by Student's t-test to see if there was a statistically significant difference between the treatment groups.

RESULTS

The selected evaluators (dermatologists) assessed the data referring to all patients in each group and imputed the scores to each pair of images (before and after treatment), as shown in table 1.

Based on the scores, we calculated the frequencies of grades indicating worsening of the condition (from -3 to -1, that is, negative scores), no changes (score zero), or improvement of the condition after the treatment (from 1 to 3, that is, positive scores). The frequency ratio by treatment group is shown in graphic 1.

Only the control group showed worsening scores. Also, the treated group (group 2) had a higher percentage of patients with clinical improvement (70%) than group 1 (54%).

After a statistical comparison of the scores between the treatment groups by Student's T-test for independent samples, we found that there was a statistically significant difference between the treatments regarding the scores obtained ($p=0.017$), proving the greater efficacy of the treatment using the combination of intradermotherapy, microneedling, and ampoule (group 2) when compared to isolated intradermotherapy (group 1).

Tablela: Scores assigned by the evaluators to standardized photos and clinical findings of patients in each experimental group.

Patient	Group	Hair loss improvement scores				
		Evaluator 1	Evaluator 2	Evaluator 3	Evaluator 4	Evaluator 5
F.S.J.	2	2	3	2	2	3
I.C.M.	2	3	2	2	1	2
R.M.C.	2	1	2	2	2	2
D.C.S.C.	2	2	2	0	1	1
K.A.	2	0	0	1	0	0
F.M.R.	2	1	0	0	0	0
R.R.T.	2	0	0	0	0	0
G.L.M.F.	2	1	1	0	1	1
R.M.	2	2	1	1	2	2
E.R.G.	2	1	3	1	1	2
D.R.M.	1	0	0	-1	0	0
A.G.V.	1	2	1	1	2	2
H.W.S.C.	1	2	2	0	1	2
I.A.S.J.	1	-1	0	-1	0	-1
T.G.F.	1	0	0	-2	-1	-1
K.C.B.	1	1	1	2	1	0
R.M.S.	1	0	-1	-2	-1	0
P.S.M.S.F.	1	2	2	2	2	3
C.H.M.C.	1	2	1	1	1	1
N.M.	1	2	0	1	2	2

Caption:
Group 1: patients submitted to intradermotherapy (control)
Group 2: patients undergoing associated therapy of intradermotherapy, microneedling, and sterile topical solution, whose active components are Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract, and Silanediol salicylate (investigational product)

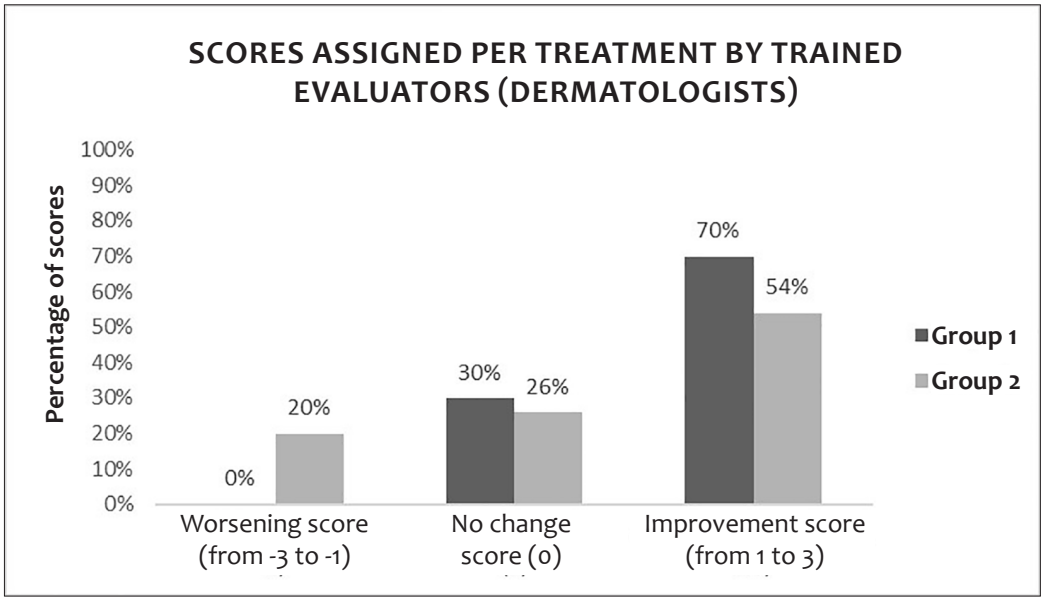
DISCUSSION

Physicians have several therapeutic options to manage disorders associated with hair loss. The present investigational product differs from other therapies as it contains in its composition biomimetic peptides (also called bioactive peptides) such as Copper tripeptide-1 and Octapeptide-2, which act by mimicking the structure and/or activity of growth factors, with better stability, greater specificity, and lower cost than the growth factors themselves.[6-7] These actives interact with the cells of the dermal papilla and capillary bulge, activating the proliferative phase of the hair.[6]

Copper tripeptide-1 stimulates stem cells in the hair follicle leading to increased size and promoting metalloproteinases and angiogenesis.6-8 Octapeptide-2 is a thymosin-b4 biomimetic peptide – a hair growth stimulator. It boosts hair growth by enhancing angiogenesis and promoting the migration of stem cells and their immediate progeny to the follicle base, causing differentiation and extracellular matrix remodeling. [6-8]

In addition to the biomimetic peptides, the ampoule used Chondrus crispus extract in its composition. Chondrus crispus is a species of red seaweed whose extract is rich in bioactive compounds, such as proteins, peptides, amino acids, lipids, polyphenols, and polysaccharides. Among the predominant components, there are flavonoids, phenols, and tannins. This extract has antioxidant, anti-free radical, and anti-inflammatory properties, contributing to the improvement of alopecia.[9]

Microneedling is a minimally invasive and promising technique that uses fine needles to promote micropunctures in the skin or scalp. It is used in several types of treatments, including in



Graphic 2:
Group 1 = patients submitted to intradermotherapy (control)
Group 2 = patients undergoing associated therapy of intradermotherapy, microneedling, and sterile topical solution, whose active components are Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract, and Silanediol salicylate (investigational product)

patients with androgenetic alopecia, and can be associated with other therapies, such as topical minoxidil.[10-11]

The microlesions promoted by microneedling cause platelets and neutrophils to release growth factors, which, in turn, stimulate the repair and growth of skin structures. Also, they promote vasodilation and the migration of keratinocytes and fibroblasts to heal microlesions.[10]

In patients with androgenetic alopecia, microneedling activates skin revascularization, which can stimulate capillary growth by increasing follicle nutrition.[10] According to Fertig *et al.*, microneedling increases capillary growth in patients with androgenetic alopecia by releasing platelet-derived growth factor, epidermal growth factor, and capillary bulge activation, triggered by the healing response of micropunctures. Also, there is increased expression of Wnt proteins, which stimulate dermal papillary stem cells and growth.[11]

The association between microneedling and topical minoxidil was superior to minoxidil and microneedling monotherapy, showing that it is an interesting tool for enhancing therapeutic efficacy.[10-12] The effective association between microneedling and topical active component also proved to be accurate in the present study, which obtained a better result in the combined therapy of intradermotherapy and microneedling with the application of a topical solution containing active principles for hair growth compared to intradermotherapy alone. However, we understand that future research should compare it with another control group associating intradermotherapy and microneedling to verify the real relevance of the topical active solution.

The therapeutic association studied showed statistically significant results in the men evaluated, making it relevant to assess the behavior of this protocol in women and/or patients affected by other hair loss conditions in future research.

CONCLUSION

When comparing the clinical findings and the standardized photos of both treatment groups, it was possible to verify that there was a statistically significant difference between the treatments regarding the scores obtained ($p=0.017$), proving greater efficacy of the treatment by associated intradermotherapy therapy, microneedling, and topical solution containing Octapeptide-2, Copper tripeptide-1, Chondrus crispus extract and Silanediol salicylate (group 2) when compared to intradermotherapy alone (group 1). In combined therapy, none of the evaluated patients showed worsening of the baldness during the treatment period, and 70% of these showed visible improvement in hair loss, corresponding to a very expressive result.

Future research should compare microneedling alone and microneedling associated with the topical active substance to quantify its real influence to improve androgenetic alopecia.

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Approval of the final version of the manuscript; study design and planning; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases.

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