Original Articles

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Rejuvenation of aging hands with a hyaluronic acid soft tissue filler range: efficacy, safety and patient satisfaction during six months

Rejuvenescimento das mãos com preenchedores cutâneos à base de ácido hialurônico: eficácia, segurança e satisfação dos pacientes durante seis meses

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ABSTRACT

Introduction: Hyaluronic acid-based soft tissue fillers are considered one of the treatment options for hands rejuvenation.

Objective: To evaluate the efficacy a range of soft hyaluronic acid (HA) gels in women with loss of adipose tissue and dermal reabsorption as a sign of aging hands.

Methods: Fifteen subjects received treatment with two firmer HA gels combined with the softest gel of the range (group 1). Fifteen subjects received the two firmer HA gels only (group 2). Efficacy and safety assessments were performed at month one, three and six. Patient satisfaction and self-assessment questionnaires were applied.

Results: Most subjects were Caucasian (Fitzpatrick skin type III and IV) with a mean age of 56.6 years. Six months after treatment, all the subjects in Group 1 and 93% in Group 2 had clinical improvement; and 90% of the subjects in both groups presented global aesthetic improvement. Mild pain was reported in both groups. All related adverse events were mild or moderate.

Conclusions: Both treatments were effective and safe, and improvement was seen for up to six months after treatment. Subjects reported high satisfaction with both treatments up to the end of study.

Keywords: hand; rejuvenation; hyaluronic acid; skin aging

RESUMO

Introdução: *Os preenchedores à base de ácido hialurônico (AH) são considerados uma das opções de tratamento para rejuvenescimento das mãos.*

Objetivos: *Avaliar a eficácia de preenchedores de AH em mulheres com perda de tecido adiposo e reabsorção dérmica como sinais de envelhecimento no dorso das mãos.*

Métodos: *Quinze participantes receberam tratamento com dois géis de AH mais firmes combinados com o gel mais fluido da mesma linha (grupo 1), e outras 15 com dois géis de AH mais firmes apenas (grupo 2). Avaliações de eficácia e segurança foram realizadas em um, três e seis meses. Questionários de satisfação e autoavaliação foram aplicados.*

Resultados: *A maioria das participantes apresentou fototipos (Fitzpatrick) III e IV, e a idade média foi de 56,6 anos. Seis meses após o tratamento, todas as participantes do grupo 1 e 93% do grupo 2 apresentaram melhora clínica; e 90% das participantes de ambos os grupos apresentaram melhora estética global. Dor leve foi relatada em ambos os grupos. Todos os eventos adversos foram leves ou moderados.*

Conclusões: *Ambos os tratamentos foram eficazes e seguros, e foi observada melhora por até seis meses após o tratamento. A maioria dos participantes referiu alta satisfação até o final do estudo.*

Palavras-chave: *mãos; rejuvenescimento; ácido hialurônico; envelhecimento da pele*

INTRODUCTION

In the last decades, signs of aging in hands have become a common area of concern in the aesthetic dermatology field. There are three-dimensional changes in the aging process of the hands, involving bone, subcutaneous structures, such as adipose tissue reabsorption, and the skin, as decreased collagen and hyaluronic acid content.[1]

Different treatments have been reported to enhance the appearance of aging hands,[2-6] including intense pulsed light, chemical peels, microdermabrasion, and cryotherapy for pigmentation irregularities;[3,7] sclerotherapy for enlarged and visible veins. One of the most noticeable sign of aging in hands is the loss of subcutaneous fat, which can be replaced with different soft tissue fillers such as poly-l-lactic acid, calcium hydroxyapatite, and hyaluronic acid.[3,7] Hyaluronic acid (HA)-based soft tissue fillers are safe and can be considered one of the treatment options for hand rejuvenation.[8-10]

A wide variety of commercially available HA fillers exist with different characteristics and chemical properties.[11] The Emervel® (Galderma S.A., Lausanne Switzerland) range of HA soft tissue fillers has been approved in Europe since 2008 and in Brazil since 2011. Although the safety and efficacy of the these products have been reported for full face rejuvenation,[12,13] no previous clinical trials have assessed their efficacy for hand rejuvenation. All the five products of this range have been developed with the same concentration of HA (20mg/mL), varying the degree of cross-linking, particle size and gel firmness.[14] Except for Emervel® Touch, all fillers of this range are presented in two different formulations either without or with lidocaine (L).[14]Both Emervel® VolumeL and Emervel® DeepL are transparent, bioresorbable gels composed of cross-linked HA with 0.3% (w/v) lidocaine hydrochloride. They have medium to large sized particles.[14] Facial indications, such as cheek and tear troughs, have been treated with these two products.[12,15] Among the Emervel® range of products, there is no specific filler for a given indication in full-face rejuvenation so the choice of filler can be tailored to the individual.[12]

Emervel® VolumeL and Emervel® DeepL are firmer gels than Emervel® Touch and are considered suitable to restore loss of subcutaneous tissue in hands. Emervel® Touch, on the other hand, is a softer gel.[14] It is ideally suited to treat superficial wrinkles. Due to the lack of data on the use of these fillers in hands, this trial was designed to evaluate the efficacy of the two firmer HA gels (Emervel® VolumeL and Emervel® DeepL) with or without concomitant injections of the HA softer gel (Emervel® Touch) in women with loss of adipose tissue as a sign of aging hands.

MATERIAL AND METHODS

Study design and Subjects

This single center, phase IV, randomized, investigator-blind, parallel-group study was conducted at the Brazilian Center for Studies in Dermatology, Porto Alegre, Brazil. The study was reviewed and approved by the Ethics Committee of *Moinhos de Vento Hospital* prior to initiation and conducted in accordance with all ethical principles applicable to clinical research and in compliance with local regulatory requirements. Five visits were performed for each subject: screening; baseline/procedure, and follow-up visits one, three and six months after the procedure.

The main inclusion criteria were women between 18 and 65 years, having never performed soft tissue augmentation on the dorsum of the hands, having at least grade 2 according the 5-point Validated Hand Grading Scale[16] (Table 1), and presenting similar loss of fatty tissue on the dorsum of the both hands.

Treatment

Eligible subjects were randomly allocated to one of the two groups at 1:1 proportion. Group 1 received treatment with the firmer HA gels, one in each hand, combined with the softer gel. And Group 2 received the firmer HA gels, one in each hand, without the softer gel. Firmer gels were randomly dispensed to either right or left hand for both groups. A touch up could be done 28 days after the procedure if considered necessary by the investigator.

The firmer HA soft tissue fillers were injected in the subcutaneous tissue with a 7 cm 21G cannula. The product was uniformly placed between the tendons using retrograde injections. The softer gel, only for group 1, was injected in the mid dermis with serial punctures, using the 30G needle provided with the product.

Assessments

The severity of fat tissue loss and the aesthetic aspect of subjects' hands were assessed by a blinded investigator using the Validated Hand Grading Scale (VHGS) (Table 1)[16] and the Global Aesthetic Improvement Scale (GAIS) (Table 2).[17]Fat tissue loss was assessed at baseline and follow-up visits and the aesthetic improvement was assessed in follow-up visits (month 1, 3 and 6).

Subjects completed a global satisfaction and self-assessment questionnaire one, three and six months after treatment. Subjects rated skin elasticity, moisturizing, beauty, and volume augmentation on a 10-point scale from 1 (little) to 10 (much), and stated percentage improvement for skin elasticity, moisturizing, beauty and volume augmentation.

Table 1: Validated Hand Grading Scale (VHGS)

Grade	Description
0	No loss of fatty tissue
1	Mild loss of fatty tissue and slight visibility of veins
2	Moderate loss of fatty tissue and mild visibility of veins and tendons
3	Severe loss of fatty tissue and moderate visibility of veins and tendons
4	Very severe loss of fatty tissue and marked visibility of veins and tendons

The blinded investigator asked the subjects to assess pain sensation using the visual analogue scale (VAS) for pain assessment related to the procedure and the touch up. As in Jensen *et al*,[18] 0 - 4 mm were considered no pain; 5 - 44 mm mild pain; 45 - 74 mm moderate pain; and 75 - 100 mm severe pain. All adverse events were recorded throughout the study. Standardized photographs were taken at each visit.

Statistical Methods

Considering that this was an exploratory study, a convenience sample size of 30 subjects was defined. Data were expressed by mean and standard deviation or percent.

RESULTS

All the 30 enrolled women completed the study. Overall, most subjects were Caucasian (phototypes III and IV) with a mean age of 56.6 years. Most subjects presented with severe loss of fatty tissues with a mean of VHGS of 3.1 for Group 1 and 2.9 for Group 2. The two groups were comparable in terms of demographic and clinical baseline characteristics. Demographic data and clinical baseline characteristics are shown in Table 3.

All the subjects received 2 mL of Emervel® VolumeL and 2 mL of Emervel® DeepL, one in each hand. Subjects of Group 1 received also 1 mL of Emervel® Touch in each hand concomitantly to the treatment with the firmer gels. A touch up with 1 mL of each product was performed in all the subjects.

All the subjects presented at least a 1-grade improvement in VHGS at one and three months after treatment. Six months after treatment, all the subjects in Group 1 still had at least a 1-grade improvement in VHGS and 93% in Group 2 (Figure 1). Six months after treatment, aesthetic appearance was much or very much improved for about 90% of the subjects of both groups, according to the GAIS (Figure 2). Standardized photographs show the visual appearance of the back of the hands of Group 1 and Group 2 before and after treatment (Figures 3 and 4).

At the end of the study (month 6), the high level of efficacy was confirmed by overall satisfaction; 86.6% of Group 1 were satisfied with the treatment, and 100% in Group 2 (Figure 5). Six months after treatment, subjects of both groups graded their skin elasticity as 7, on the 10-point scale. Skin moisturizing, beauty, and volume, were graded 6.4, 7.2 and 7.1, respectively, by the subjects of Group 1. And graded 6.9, 7.2 and 7.1 by the subjects of Group 2.

After each injection, mild pain was reported in both groups. The mean score of pain using the VAS never exceeded 40 mm in any group. Overall, no particular safety concerns were observed and no serious adverse events or device complaints were reported during the study. Eight subjects presented procedure-related hematomas, 6 from Group 1 and 2 from Group 2. Ten subjects presented adverse events related to the product, 8 from Group 1 and 2 from Group 2. The most frequent adverse events were nodulation, which occurred in 6 subjects (20% of the patients), all from Group 1, and edema which occurred in 5 subjects (17%), 3 from Group 1 and 2 from Group 2. The duration of the nodulations observed lasted from 2 weeks to less than 6 months. All resolved spontaneously. Edema lasted from 2 to 10 weeks, and resolved spontaneously in 3 patients, whereas two patients required treatment with oral corticoids. Pruritus and hyperemia occurred in two subjects (7%) of Group 1, and only one patient (Group 2) reported pain up to 3 days after the procedure.

DISCUSSION

This study assessed the efficacy and safety of two firmer hyaluronic acid gels combined with or without a softer gel of a specific range of soft tissue fillers, for hand rejuvenation. Both treatments were effective and results were seen for up to six months after treatment.

All the subjects in both groups showed clinical improvement one and three months after treatment, and the great majority showed improvement up to six months. Aesthetic evaluations also suggest high efficacy of the product, since about 90% of the subjects showed much or very much improvement in the appearance of their hands at the end of the study as assessed by a blinded evaluator.

Subject reported outcomes also indicate treatment efficacy for both groups. More than 85% percent of subjects were still satisfied six months after treatment. Results show a slightly higher satisfaction in Group 2.

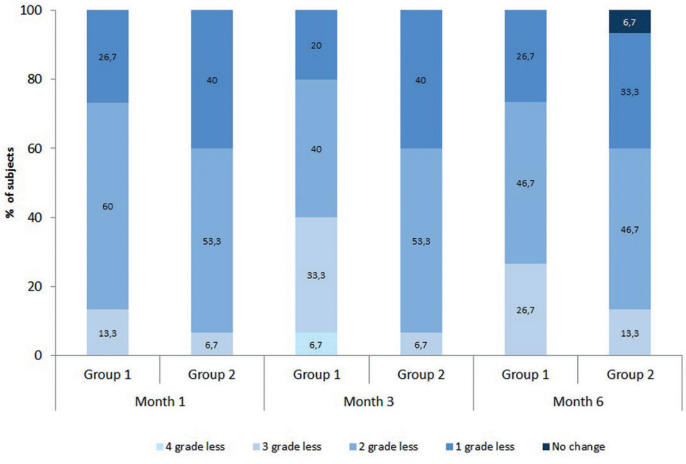
Previous studies[8-10] evaluated the safety and efficacy of soft tissue augmentation in hands with different types of HA fillers. A HA filler was shown to be more efficacious than collagen for reducing signs of intrinsic aging in hands.[9] Similarly to our study, Brandt and colleagues also showed a six-month clinical effect of a HA filler.[8] However, their results regard the use of a small particle HA gel alone.

Table 2: Global Aesthetic Improvement Scale (GAIS)

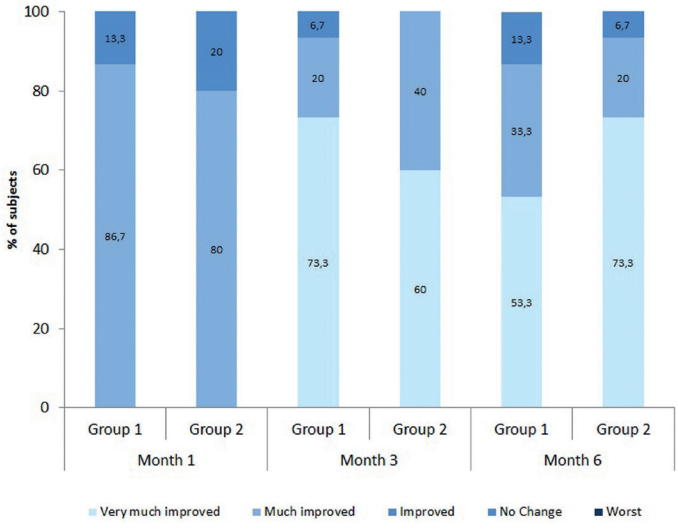
Grade	Description
Very much improved	Optimal cosmetic result for the implant in this patient
Much improved	Marked improvement in appearance from the initial condition, but not completely optimal for this patient. A touch-up would slightly improve the result
Improved	Obvious improvement in appearance from the initial condition, but a touch-up or retreatment is indicated
No change	The appearance is essentially the same as the original condition
Worse	The appearance is worse than the original condition

Table 3: Demographic and baseline clinical characteristics

		Group 1	Group 2	Total
Gender	Female	15 (100.0%)	15 (100.0%)	30 (100.0%)
Age (years) mean±SD		58.3 ± 5.5	54.9 ± 6.9	56.6 ± 6.3
Race	Caucasian	15 (100.0%)	14 (93.3%)	29 (96.7%)
	Black	0 (0%)	1 (6.7%)	1 (3.3%)
Skin phototype	II	1 (6.7%)	3 (20.0%)	4 (13.3%)
	III	12 (80.0%)	5 (33.3%)	17 (56.7%)
	IV	2 (13.3%)	6 (40%)	8 (26.7%)
	V	0 (0.0%)	1 (6.7%)	1 (3.3%)
VHGS (loss of fatty tissue)	2: Moderate	1 (6.7%)	4 (26.7%)	5 (16.6%)
	3: Severe	11 (73.3%)	8 (53.3%)	19 (63.3%)
	4: Very severe	3 (20.0%)	3 (20.0%)	6 (20.0%)
	Mean	3.1	2.9	3



Graph 1: Validated Hand Grading Scale at each follow-up visit



Graph 2: Global Aesthetic Improvement Scale. Investigator rated improvement up to 6 months to all the subjects

Soft gels have been used for face and hand rejuvenation and, to improve skin quality.[19,20] These products are applied in the mid-dermis using a multi puncture technique. Two studies have demonstrated global aesthetic improvement of aging hands for up to one year after three monthly injections of a stabilized hyaluronic acid gel (Restylane Vital®, Galderma S.A., Lausanne, Switzerland).[19,20] Both studies assessed the effects of this product used alone. In the present study, we observed that the HA softer gel combined with the firmer HA fillers resulted in no additional improvement in hand appearance.

Subjects reported high satisfaction with both treatments in the present study up to six months after treatment. Long-term subject satisfaction is commonly observed with the use of HA-based fillers for facial or hand rejuvenation.[8,12,13,19-21] Since hyaluronic acid fillers are expected to last up to 12 months,[22-24] probably the patients could be satisfied with the results after the 6-month follow up period.

All the subjects received lidocaine-containing gels. Mild pain was observed for both groups at the moment of the injections in the treatment and also touch-up procedures, as expected with lidocaine HA fillers,[25-28] since the anesthetic effects take a few minutes to occur. Products showed a good safety profile. Only transient procedure-related adverse events at the injection site were seen, such as hematoma, nodules, edema, pruritus and erythema. These adverse events may be expected after treatment with HA-based soft tissue fillers[12,13,19,20,29], and all disappeared

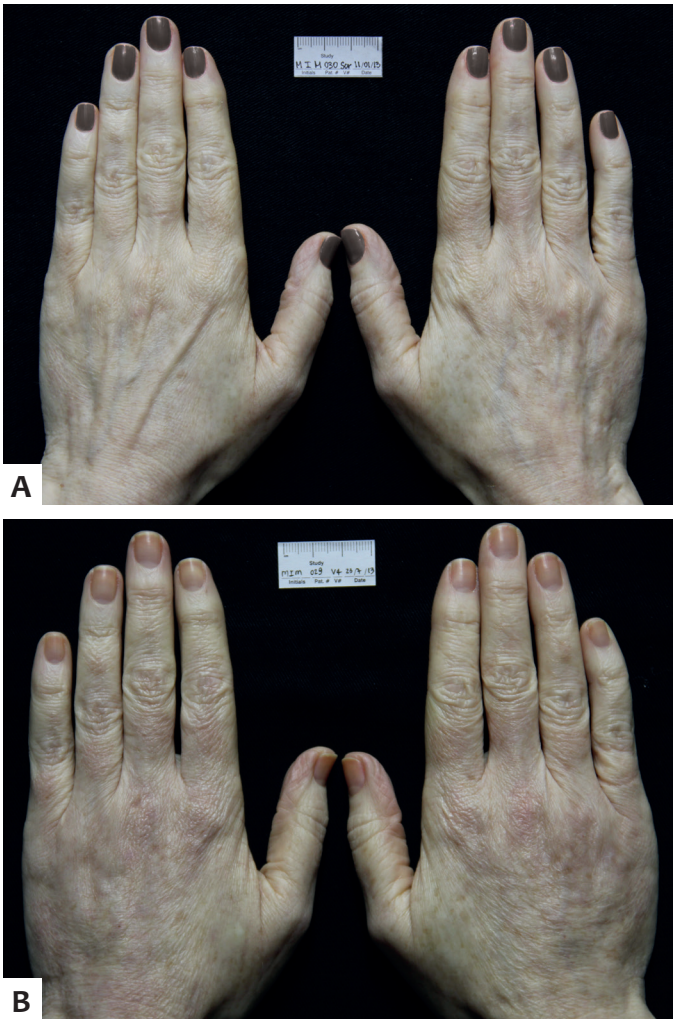


Figure 1: Photographs of one patient of Group 1 before treatment **A,** and six months after treatment **B**

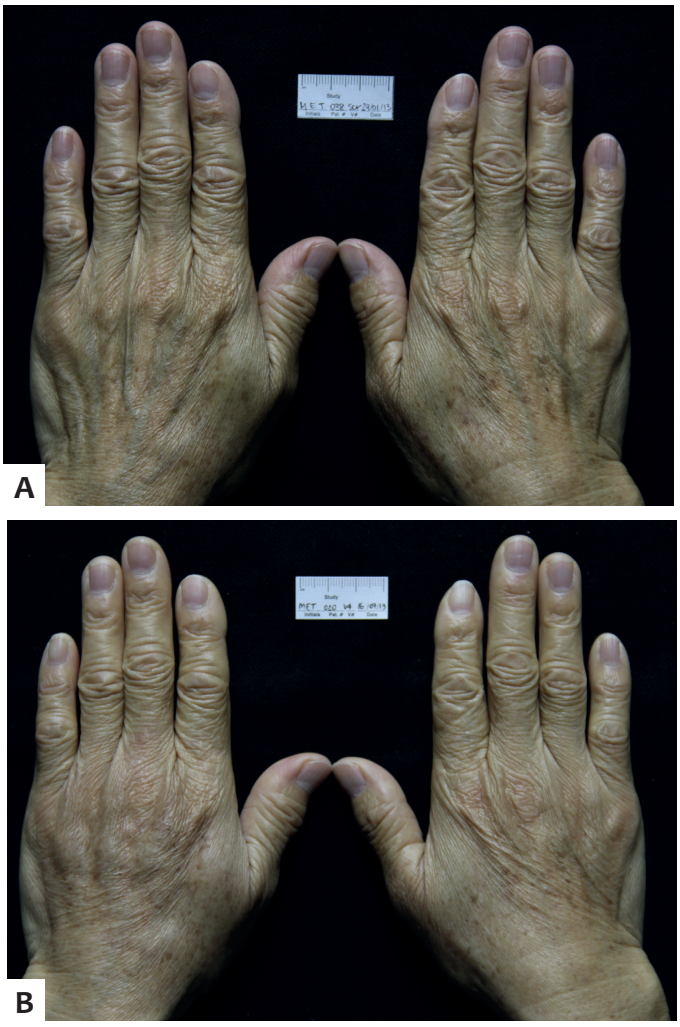
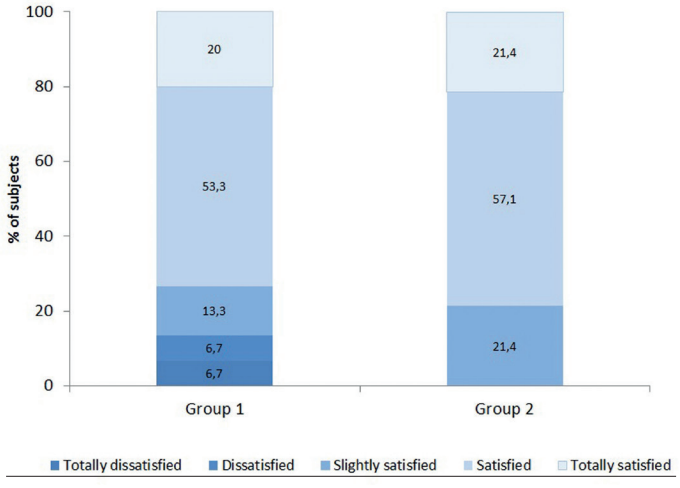


Figure 2: Photographs of one patient of Group 2 before treatment **A,** and six months after treatment **B**



Graph 3: Subject satisfaction 6 months after treatment

during the study. As expected, there were more AEs related to the injection procedures in Group 1, since more injections were done in this group.

This is an exploratory study, thus there was no calculation to define the sample size. Nevertheless, results can show aesthetic improvement of aging hands for both groups compared to baseline.

CONCLUSIONS

The present results demonstrate that the HA fillers used in this study are safe and efficient for rejuvenation of aging hands. Patients of both groups, either receiving additionally the softer gel or not, had improvement in the visual aspect of the aging hands. Emervel® fillers provide physicians with another possible option for this increasingly popular cosmetic treatment, but more studies could be developed to evaluate the efficacy and safety profile of these products. ●

DECLARATION OF PARTICIPATION:

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Data collection, manuscript writing and final review

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