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A five-patient prospective pilot study of a polycaprolactone based dermal filler for hand rejuvenation

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Summary

Background Hand rejuvenation is becoming more popular as a complementary procedure to facial treatments. Current options include the relatively invasive lipofilling and the less invasive dermal fillers treatments, of which the latter often is too short lasting. An ideal product would therefore be minimally invasive, however, providing longer lasting results.

Objectives The objective of this pilot study is to evaluate the safety and efficacy of a polycaprolactone based dermal filler for hand rejuvenation.

Methods The dorsum of the hands of five subjects was treated with 1.0 mL polycaprolactone based dermal filler per hand. Subjects were seen for follow-up visits after 1, 4, 16, and 24 weeks.

Results The results showed consistent and high patient satisfaction throughout the duration of the study using a Visual Analog Scale. Satisfaction was rated at 82% at 24 weeks and patients were 88% likely to return for repeat treatments on average. On the subject GAIS assessment, all subjects reported an improvement compared to pretreatment throughout the duration of the study. The physicians' GAIS results were very much improved (90%) and much improved (10%) compared to pretreatment throughout the 24 weeks follow-up.

Conclusions The data of this small pilot suggest that the polycaprolactone based dermal filler is safe, well tolerated and effective for hand rejuvenation, and potentially offers a valuable addition to the current treatment armamentum. Additional studies in a larger patient population should be performed to confirm these findings.

Keywords: biostimulator, hand grading scale, injectable, polycaprolactone, PCL, rejuvenation

Introduction

As well as the face, hands show signs of aging caused by unavoidable sun exposure and intrinsic changing of the dermis. The aged hand is characterized by the loss of subcutaneous fat, collagen, and its elasticity resulting in a more translucent and thinning skin, making the underlying structures like bone, tendons, and veins more visible.

The hyperpigmentation, change in skin thickness, and the fine wrinkles of the dorsum of the hand can be treated with different types of lasers, chemical peels, and intense pulsed light.[1] To correct the volume loss of the hands and to improve the total skin appearance, autologous fat replacement,[1] and injectable dermal fillers, such as hyaluronic acid (HA),[1,2] calcium hydroxylapatite (CaHA),[1,3,4] and poly-L-lactic acid (PLLA),[1,5]

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can be used. This article describes the use of a polycaprolactone based dermal filler for hand rejuvenation.

Polycaprolactone based dermal filler

A biostimulating dermal filler based on polycaprolactone (PCL) microspheres (Ellansé™, AQTIS Medical, Utrecht, The Netherlands) was recently introduced to the esthetic market. The product consists of 30% non-cross-linked PCL microspheres (25–50 μm) and 70% aqueous carboxymethylcellulose (CMC) gel carrier, and is available in four versions. It is the first dermal filler based on PCL microspheres.

In a clinical trial for the correction of nasolabial folds, it was found that the PCL-based dermal filler is safe and well tolerated for facial treatment.[6]

Polycaprolactone and CMC individually have excellent and proven biocompatibility profiles and have been used successfully in numerous medical devices, such as dermal fillers, oral and maxillo-facial surgery, orthopedics, wound dressing, and controlled drug delivery.[7–13]

Polycaprolactone is a medical polymer, which is completely bioresorbable as shown using ^{3}H-labeled and C^{14}-labeled PCL.[14,15] The PCL-chains undergo chain scission through hydrolysis, resulting in hydroxycaproic acid and water, which are resorbed through metabolic pathways and readily excreted.[14–18]

After injection, the CMC gel-carrier is gradually resorbed by macrophages over a period of several weeks, during which the smooth and spherical-shaped PCL microspheres stimulate neocollagenesis to replace the volume of the resorbed carrier.[19]

The objective of this pilot study was to assess the safety, efficacy, patient and physician satisfaction and duration with the PCL dermal filler on the dorsum of the hands. Based on the longevity shown in clinical reports, this product may contribute to the current treatment options by providing minimally invasive, longer lasting results.

Methods

Patient Population

The study enrolled five female subjects between the ages of 54 and 76 years. Subjects were enrolled if both hands of the patient had a rating of three to four on the Hand Grading Scale (HGS),[20] i.e. severe to very severe loss of fatty tissue and moderate to marked visibility of veins and tendons.

The study followed the principles of the declaration of Helsinki and was consistent with good clinical practice guidelines.

Study Design

In this pilot study, subjects received the M-version of the product (PCL-2) in the dorsum of both hands. All subjects received one single treatment. No touch up was performed during the study. Subjects then returned for both physician and subject evaluation at 1, 4, 16, and 24 weeks. For the assessment of safety and efficacy, photographs were taken of the dorsum of the hand pretreatment and at every return visit. The evaluation was performed using the HGS, the Global Aesthetic Improvement Scale (GAIS) for efficacy, and a Visual Analog Scale (VAS) to determine patients' satisfaction and likelihood to return.

To be included in the study, subject had to be 18 years of age or older, have severe to very severe loss of fatty tissue and moderate to marked visibility of veins and tendons as determined by a HGS score of 3 or 4 in both hands at the pretreatment evaluation. Subjects had to sign a written informed consent and understand and accept the obligation not to receive any other procedures in the dorsum of the hands for 12 months.

Exclusion criteria were as follows: Subjects who had planned activities during study that could interfere with treatment or that impose significant force to the hands; subjects with a history of hypertrophic scarring; subjects with a known bleeding disorder; subjects that received, or anticipated to receive antiplatelets, anticoagulants, thrombolytics, vitamin E or anti-inflammatories within 2 weeks pretreatment; subjects receiving systemic corticosteroids; subjects with a history of chronic or recurrent infection or inflammation that would preclude participation in the study; subjects who have a known hypersensitive to any of the component of PCL dermal filler; subjects who previously had any dermal filler or surgery in the dorsum of the hand; female patients of child bearing potential not using medically effective birth control, or is pregnant or lactating.

Pretreatment

Prior to participation in the study, the subject received patient information and signed and dated the study consent. Prior to treatment, subjects received a brief general examination, including medical history and survey of current medications.

Pretreatment photographs of the dorsum of the hands were taken for each subject and used throughout the course of the study to assist the subject and

investigator in completion of the GAIS at the follow-up visits.

Treatment

Polycaprolactone-2 was placed directly in the dorsum of both hands using a blunt cannula (22G x 70 mm). No topical or injectable anesthetic was used. Neither was PCL-2 premixed with an anesthetic agent. The cannula entry point was determined away from any visible veins, approximately in the transition from the wrist to the hand, at the level of the superior row of carpal bones. After being cleaned with povidone–iodine solution, the skin was elevated with two fingers, raised above the vessels and the underlying anatomical structures, and pinched using a 22G x 30 mm (BD Microlance™ 3) sharp needle at a 45° angle. The 22G x 70 mm blunt cannula (Index, France) allows an easily flow of the product and the length allows the covering of the complete dorsum of the hand from only one entry point. After gently progressing the cannula from the entry point along the back of the hand until it reached the interdigital space between the fifth and fourth finger, an amount of 0.1–0.3 mL was injected in a retrograde fashion. Without losing the plane, the cannula is gently pushed forward again to the space between the fourth and third finger and withdraw injecting another 0.1–0.3 mL of the product. The same movements are repeated between the third and second finger and the first and second, in total of four lines of product. All subjects received one injection treatment during the course of the study and received a fixed amount of 1.0 mL PCL-2 in each hand. No touch up was performed at any follow-up visits. After injection, the dorsum of the hand was massaged with movements from the wrist to the fingers, and circular movements. The massaging continued until the product was optimally distributed in each hand.

Digital photographs were taken pretreatment and on each follow-up visit, using a standardized photographic setup. The subjects were evaluated for ecchymosis, edema, erythema, infection, keloid formation, hypertrophic scarring, hyper- or hypopigmentation, nodules, and other side effects on each visit. All treated subjects were seen for follow-up visits after 1, 4, 16, and 24 weeks. At each follow-up visit, physicians' and patients' efficacy for each hand was determined using a GAIS assessment. The patients' satisfaction and likelihood to return was determined using a VAS assessment. A questionnaire was complete at each visit regarding possible side effect.

Results

Effectiveness

The overall change in appearance of the treated hands from its pretreatment condition is determined using the validated Global Aesthetic Improvement Scale (GAIS). A summary of the physicians' GAIS scores obtained is depicted in Table 1. On the physician GAIS assessment, subjects were evaluated as much improved (10%) or very much improved (90%) at 24 weeks compared to pretreatment.

On the subject GAIS assessment, 100% of the subjects reported an improvement at 24 weeks compared to pretreatment. The subject GAIS results were very much improved (90%) and much improved one week after treatment, change to very much improved (60%), much improved (10%), and improved (30%) at 24 weeks after treatment.

Patient Satisfaction

Patient satisfaction was recorded using a VAS questionnaire. Subjects were asked about their overall satisfaction with treatment results and the likelihood of returning for additional treatment with the product injected into the dorsum of their hands.

Patients rated their satisfaction with the PCL-2 at 82% at 24 weeks, and their likelihood to return for additional treatments at 88% (Table 2).

Table 1 Physician Evaluated GAIS

GAIS Score Change (%)	0 week*	1 week	4 week	16 week	24 week
Very Much Improved	100	90	90	90	90
Much Improved	0	10	10	10	10
Improved	0	0	0	0	0
No Change	0	0	0	0	0
Worse	0	0	0	0	0

*immediately after treatment.

Table 2 Patient satisfaction and likelihood to return using the Visual Analog Scale questionnaire

	Patient satisfaction (%)	Likelihood to return (%)
1 week	91	96
4 weeks	85	94
16 weeks	81	90
24 weeks	82	88

Figure 1 shows a representative result of (a) pretreatment, (b) 16 weeks postinjection, and (c) 24 weeks postinjection.

Safety

No serious adverse events were reported during the 24-week follow-up. Two subjects reported mild swelling of the dorsum of the hand 24 h postinjection, which resolved within 48 h using oral ibuprofen 600 mg twice a day. No lumps, nodules, or other late adverse events were observed during the 24-week study.

Discussion

Injection procedure

The advantage of using a cannula over the traditional needle is the a-traumic injection and the ability to volumize the entire dorsum of the hand using only a single entry point. In this study, subjects received 1.0 mL PCL-2 in each hand, and no additional injection was offered at the follow-up visits. In clinical practice, more filler can be injected if needed, keeping in mind the maximum 1:1 correction of the PCL dermal filler. A slight under-correction may be preferred due to the strong neo collagenesis response.

Effectiveness

On a highly mobile area, such as the hand, it is important that the injected product remains in place in the treated area and is unlikely to move or migrate. The PCL microspheres stimulate neocollagenesis embedding the microspheres in a matrix of body's own new collagen and anchoring the microspheres in place, as shown elsewhere.[19] As a result, there is minimal chance of migration of the material.

The PCL dermal filler was not premixed with a lidocaine-solution, which is a common procedure for e.g. CaHA dermal filler during hand rejuvenation. The main purpose is to lower the viscosity of the CaHA carrier for better moldability. Due to the viscosity and elasticity of the PCL dermal filler, the substance is already easy to inject and to spread out over the dorsum of the hand. Therefore, no dilution is required to obtain the desired result. Even though no anesthetic was used and the injection procedure was well tolerated.

On both the physician as the patient GAIS assessment, all subjects showed an improvement at 24 weeks compared to pretreatment. The patient satisfaction ratings demonstrated consistent and high satisfaction throughout the duration of the 24 weeks study. Also, the likelihood to return for additional treatments at 24 weeks showed high ratings confirming the satisfaction results and suggesting a high patient retention.

Comparison

The hand rejuvenation using the PCL-2 dermal filler may offer some advantages over other treatments options. Autologous fat treatment consists of harvesting, preparing, and finally injection of the fat in the dorsum of the hand.[1] This procedure is more time consuming and requires a sterilized environment. The volumizing effect with autologous fat is widely variable, ranging from 4 months to 3 years.[1]

Hand rejuvenation with PLLA need some time until the volumizing effect appears, as the product lacks a volumizing gel-carrier.[1,5] On average, three to four treatment sessions are required to obtain the desired effect, and the longevity of PLLA in hand rejuvenation is variable. The PCL filler provides an immediate effect and providing a choice in longevity.

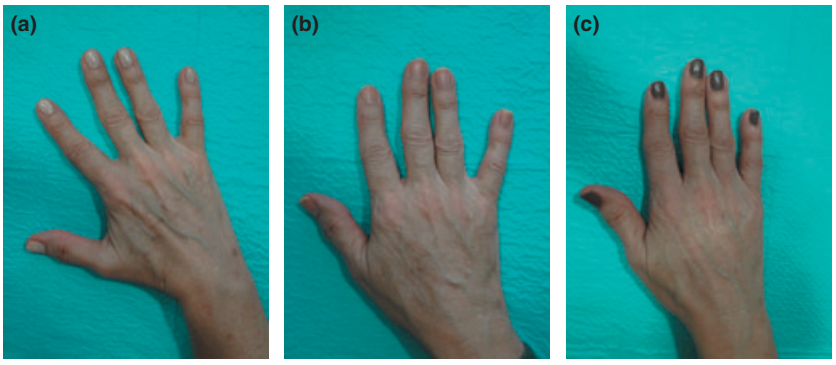

Figure 1 A representative result of (a) pretreatment, (b) 16 weeks postinjection, and (c) 24 weeks postinjection.

The longevity of HA products usually is between 6 and 9 months.[1,2] The PCL filler has a tunable longevity, depending on the type of product used.

Calcium hydroxylapatite, also widely used for hand rejuvenation, may need dilution with a lidocaine-solution to obtain optimal viscosity. The longevity of CaHA lies in the range of from 9 to 12 months in most cases.[1,3,4] This premixing is not required with the PCL filler. The longevity of PCL filler in hands seems to be tunable, depending on the version used, although this needs to be confirmed over a longer follow-up period.

Conclusion

polycaprolactone dermal filler, a biostimulator, was found to be a safe and well-tolerated filler for hand rejuvenation. Due to the viscosity and elasticity of the substance, the dermal filler can easily be injected and with manual massage be spread out naturally over the treatment area of the hand. There were no signs of product movement or displacement, eventually due to the neocollagenesis process anchoring the microspheres, even in the highly mobile hands. The limitation of this study is the small number of patients used. However, the efficacy data and patient satisfaction observed in this study merit further investigation. It is expected that the PCL dermal filler may become an attractive option for hand rejuvenation.

Declaration of interest

Dr. Figueiredo has received research, speaking and consulting support from AQTIS Medical.

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