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A novel dermal filler based on polycaprolactone (PCL) has been introduced to the aesthetic market. A recently published study has shown that the PCL-based dermal filler induces neocollagenesis in rabbit tissue, a process associated with improvement in the skin's appearance. In this pilot study we investigated if the PCL-based dermal filler induces neocollagenesis in human tissue by using histological analysis. Two patients that were enrolled in the study, and were willing to undergo temple lifting surgery, were injected intra-dermally with the PCL-based dermal filler. 13 months post-injection, biopsies were obtained for subsequent histological analysis. Histological analysis with tissue obtained from the biopsies (13 months post-injection) revealed that the PCL-based dermal filler shows collagen formation around the PCL particles and therefore supports similar findings previously shown in rabbit tissue. In agreement, PCL particles are maintained in their original state 13 months post-injection.

Keywords: neocollagenesis, PCL, polycaprolactone, tissue augmentation

Introduction

As an alternative to invasive and relatively costly plastic surgery, a very popular non-invasive procedure for soft tissue augmentation can be performed with the use of injectable fillers, which range and composition expanded dramatically in the last decades.

Generally, the range of fillers that are currently on the market can be distinguished in biodegradable (e.g. hyaluronic acid (HA)), biodegradable collagen stimulator (calcium hydroxylapatite (CaHA) and poly-L-lactic acid (PLLA)), and non-biodegradable products such as polymethylmethacrylate (PMMA) [1].

Biodegradable collagen stimulators are the latest next-generation dermal fillers with characteristics that can induce a process called neocollagenesis [2]. In addition to CaHA and PLLA, which both have their own efficacy and longevity profile, a promising new biodegradable collagen stimulatory filler, composed of 30% synthetic PCL microspheres and 70% aqueous carboxymethylcellulose (CMC) gel carrier (Ellansé^{tm}; Aqtis Medical, a Sinclair Company; Utrecht, The Netherlands), has recently been introduced to the aesthetic market. Its unique tuneable longevity gives the dermal filler variable durations for up to four years (Ellansé^{tm} -S (1 year), Ellansé^{tm} -M (2 years), Ellansé^{tm}-L (3 years), and Ellansé^{tm} -E (4 years) and is therefore ideal for those seeking longer-lasting results.

In a clinical trial for the correction of nasolabial folds (NLFs), it was found that the PCL-based dermal filler is safe and well tolerated for facial treatment [3]. In addition, a pilot study has shown that the PCL-based dermal filler is safe, well tolerated, and effective for hand

rejuvenation [4]. Furthermore, in a recently published study is has been shown that the PCL-based dermal filler is capable of inducing neocollagenesis in rabbit tissue [5]. However, similar data for human tissue is not yet available. Therefore, in this study, the capability of the PCL-based dermal filler to induce neocollagenesis was investigated by using histological analysis on human tissue.

Materials and methods

Patient population

Two patients willing to undergo temple lifting surgery enrolled for the study. Both patients were informed about the treatment, potential complications, and post-treatment results. Furthermore, pre-treatment written informed consent was obtained for both patients.

Exclusion criteria

Exclusion criteria for both patients were as follows: they should not have had prior soft tissue filler implant injections into the treatment sites, pregnancy, had some sort of immunodeficiency disorders and/or medication that might obscure the inflammatory response, or show any contraindication as noted in the instructions for use (IFU).

Study design

Both patients were injected intra-dermally in the temporal area just below the temple hairline with 1 cc of the PCL-based dermal filler. Temple lifting surgery, which included the tissue where the PCL-based dermal filler was initially injected, was performed after 13 months. Biopsies were taken from the removed tissue. Immediately after the biopsies were taken, the tissue specimens were placed in formalin for fixation. Haematoxylin & eosin (H&E) and Martin's

Trichrome (MT) staining was performed on the formalin fixed biopsies for subsequent histological analysis.

Results

Both patients completed the study without any treatment or post-treatment related adverse events.

Histological analysis with biopsies obtained at 13 months post-injection showed that the PCL particles were distributed mainly in the intra-dermal layer appearing as perfectly smooth, round, white spheres, measuring about 30 to 40 microns on average (Fig. 1). Furthermore, H&E (Fig 1A and 1B) and MT (Fig 1C and 1D) staining's revealed collagen deposition around the PCL spheres, including the presence of some histiocytes (Fig. 1).

Discussion

Recently, a novel biodegradable collagen stimulatory filler based on PCL has been added to the range of soft tissue fillers. Because the PCL-based dermal filler is composed of a 70% aqueous CMC gel carrier, it has a direct volumizing effect. Its secondary 'delayed' volumizing effect is based on new collagen production through the activation of neocollagenesis by the 30% synthetic PCL microspheres in the gel [5].

In this pilot study it is shown that the novel PCL-based dermal filler induces neocollagenesis in human tissue. However, a limitation of this pilot study is that the H&E and MT staining's that were used are not capable to differentiate between type I and type III collagen. To show this, a selective (immuno)histochemical procedure for collagen detection in paraffin-embedded tissue, like a picro-sirius red (PSR)

staining method, has to be performed. Nevertheless, the results extend previous findings where the PCL-based dermal filler has been shown to induce neocollagenesis in rabbit tissue [5].

Furthermore, at 13 months post-injection, the PCL particles are still in their original state without any indications of biodegradation confirming its long-lasting effect. These results are as expected because the PCL-based dermal filler variant M (Ellansé^{tm} –M) was used for this study. The M version has an expected longevity of 2 years followed by total bioresorbtion of the PCL particles [6, 7]. Due to the time point where the biospsies were taken in this study (13 months post-injection) did not exceeded 2 years, the total bioresobtion of the PCL particles has to be further investigated by analysing biopsies which are obtained · 2 years post-injection.

Results also show that the PCL particles remained well located in the dermal layer in where initial injection was performed (intra-dermally). This indicates that tissue migration of the PCL particles did not occur. The presence of some histiocytes around the PCL spheres indicates a mild inflammatory tissue response.

Conclusion

This pilot study indicates, in addition to a similar previously performed study in animal tissue, that the PCL-based filler is capable of inducing neocollagenesis when injected intra-dermally in human tissue.

Disclosure of interest

The authors report no conflicts of interest

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Figure Legend

Figure 1. Microscopic images (13 months post-injection) show PCL microspheres surrounded with collagen deposition and a mild fibroblastic and histiocytic tissue response. Staining's were H&E (A and B) and MT (C and D). Original magnifications, x 40 magnification (A and C) and x 200 magnification (B and C).