BACKGROUND

The objective of this study was to assess by histological analysis the early evolution of the tissue integration of TEOSYAL® RHA 4 compared to three other commercially available dermal fillers with similar indications for creation/restoration of facial volume by deep dermal or subcutaneous injections.

OBJECTIVE

Eight New Zealand White rabbits were injected subcutaneously with the four investigated products (6 injections of 300 μl per rabbit, Figure 1) for a total of 12 injections per product! At 3 days, 7 days, 14 days and 30 days post-injection, the products’ nodules of two animals were sampled with the surrounding tissues and histological slides were stained using the following agents: Sirius Red (Figure 3), Hematoxylin Eosin (H&E) (Figure 5a) and Masson’s trichrome (Figure 5b). Evaluations included the collagen density and fibrosis around the injection sites as well as the qualitative and semi-quantitative histologic evaluation of the local tissue effects and inflammatory response.

MATERIALS AND METHODS

Nodules sampling

46 of 48 nodules and implantation sites were positively identified and considered adequate for histological evaluation. Almost all nodules had an ovoid shape when sampled. Product A presented a few more cases of flattened ovoid shape when sampled.

Evolution of collagen with time

Collagen density was assessed from Sirius Red colored histological slides. Evolutions with time of the collagen density around the product are presented in Figure 3. Collagen production around the implants matched with a classical body response by reaching a regular increase before reaching a plateau (here from D03). The results at D03 are uncertain since some dermal filler material was lost. At 30 days after injection, all products yielded to a collagen layer that seemed to be thick and loosely organized for the products C and D, as illustrated by the representative photographs of Figure 7. The global fibrosis development was less prominent at injection sites of product A than for the other injection sites.

Inflammatory cell types evolution with time

From the HES (Figure 5a) and Masson’s trichrome (Figure 5b) colored histological slides, semi-quantitative scores were used to describe microscopic findings and particularly the level of inflammatory cells (0: absent), 1: slight, 2: moderate, 3: marked, 4: severe), Figures 4a, b, c show the evolution of the three main inflammatory cell types with time for each product.

RESULTS

Polyornphocellular (or neutrophils) which are the first responders among inflammatory cells to migrate towards the site of inflammation, decreased in quantity with time (Figure 4a). Lymphocytes or plasma cells which are major actors of the adaptive immune system response were observed at very low levels at all time points, indicating a very good tolerance to all products (Figure 4a). At D07 and other there were less inflammatory cells, with a shift towards predominantly macrophages, a cell type specialized in removal of cellular debris (Figure 4c). Although differences between groups were minimal, product A yielded to less prominent inflammatory cells at all time-points and for all cell types. Inflammatory cells seemed to be a little bit more present with product D.

CONCLUSION

To the best of the authors’ knowledge this is the first study aiming to precisely study the kinetic of the tissue response of a host within one month after a dermal filler injection. Four products indicated for creation/restoration of facial volume by deep dermal or subcutaneous injections were studied: TEOSYAL® RHA 4 (product A), TEOSYAL® Puresense Ultra Deep (product B), Juvederm® Voluma with Lidocaine (product C), Restylane Perlane® Lidocaine (product D). Throughout the course of the study, injections appeared to be well tolerated at all injection sites and with all materials. Although at a given time point differences between groups were minimal, a general trend in favor of TEOSYAL® RHA 4 (product A) was observed based on the results obtained on the 46 nodules analyzed. At each time point from D03 to D30, TEOSYAL® RHA 4 (product A) yielded to less prominent tissue reactions at injection sites than the 3 other dermal fillers tested and hence results suggest a better tissue integration. The results of this pilot study lead us to set up further investigations on a larger sample size, at a specific time point, to give enough power to achieve a statistically significant conclusion.