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ORIGINAL CONTRIBUTION

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Early and maintained application of the secretion of *Cryptomphalus aspersa (SCA)* 40% improves cutaneous healing after ablative fractional laser in skin aging

Pablo Fernandez-Gonzalez MD[1] | Maria Vitale MD[2] | M. Teresa Truchuelo MD, PhD[3]

[1]Hospital Central de la Defensa, Madrid, Spain

[2]Medical Department of Cantabria labs at Madrid, Madrid, Spain

[3]Vithas Nuestra Señora de América Hospital, Madrid, Spain

Correspondence
M. Teresa Truchuelo, Dermatologist in Vithas Nuestra Señora de América Hospital, Madrid, Spain.
Email: maytetd@yahoo.es

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Abstract

Background: Ablative fractional laser generates a regulated skin damage, which secondarily improves skin aging.

Aims: The main objective of the present study was to figure out if the adverse effects induced by laser and the skin recovery could improve with the application of a cosmetic product based on the secretion of Cryptomphalus aspersa (SCA).

Patients/Methods: A prospective double-blind controlled study with vehicle in 10 patients with skin aging. The patients received one session of fractional ablative CO_2 laser, and the formulation with SCA 40% was applied immediately and maintained throughout the 21-day duration of the study. The active treatment (SCA) was applied to one hemifacial area and vehicle to the other, and the patient acting was her own control. Clinical evaluations, dermoscopy, photography, and other parameters like cutaneous hydration, elasticity, and wrinkles were evaluated. In addition, the severity of the adverse effects was evaluated.

Results: Significant greater decrease in the density of microcolumns produced by laser was detected on the active-treated side, indicating greater and faster postprocedure recovery compared to the vehicle-treated side. In addition, side effects were reduced and some antiaging effects were more apparent on the side treated with SCA 40%.

Conclusion: SCA 40% applied immediately after ablative laser, and during the next days, it can accelerate laser-induced damage regeneration. In addition, SCA improves the cosmetic outcome after laser application.

KEYWORDS

ablative laser, CO_2 laser, laser recovery, skin aging, treatment

1 | BACKGROUND

Skin aging is a physiological process given by endogenous and external environmental factors.[1] Photoaging is characterized by smooth and deep wrinkles, xerosis, skin roughness, poikilodermia-like changes, and skin malignancy due to long-term UV exposure.[2] Skin aging treatments include topical formulations, peelings, botulin toxin, radiofrequency, hyaluronic acid, and lasers among

others. Among common laser treatments, CO_2 ablative fractional laser technology (wavelength: 10.400nm) gives energy that induces small microcolumns (MTZs: microscopic thermal zones) with surrounding intact skin. This reservoir of skin generates new skin through natural cutaneous mechanisms of healing, improving the aesthetical result.[3-5] The subsequent remodeling induces greater vascularity, nutrients influx, and collagen synthesis. In our study, patients were treated after laser with a product formulated with SCA 40%. SCA 40% is obtained from gastropods of the family *Cryptomphalus aspersa*. The composition of the product is rich in glycosaminoglycans (GAGs), proteins related to fibroblast growth factor, antioxidant enzymes. In addition, evidence has shown the wound healing capacity through stimulation of fibroblasts and keratinocytes of SCA.[6,7] Clinical and histopathology assessment of SCA effects proved that topical application may reverse some photoaging signs, increasing dermal thickness and decreasing wrinkle depth and roughness, probably due to the antioxidant and skin remodeling effect.[8-10]

2 | OBJECTIVES

The first aim of this study was to set whether SCA 40% was able to accelerate the postablative fractional laser skin recovery. Secondary determinations searched the efficacy of the cosmetic regimen in improving elasticity, firmness, and reducing wrinkles, as well as the tolerance of the product and the subjective patient and investigator determination of photoaging improvement.

3 | MATERIAL AND METHODS

This prospective, randomized, double-blind, vehicle-controlled study studied the application of SCA 40% (Endocare® Concentrate/Ampoules with SCA 40%) vs vehicle randomly assigned to right or left hemiface in 10 volunteer women, according to a randomization table obtained by computer.

Inclusion criteria were as follows: to be aged 40-65 years, to have a minimum score of 3 according to Rao-Goldman scale, no previous treatments 3 months before nor concomitant application of topical or systemic treatments, absence of pregnancy, and no allergies to the components of the product. They understood and signed the informed consent. The study was approved by an ethics committee and/or follows the tenets of the Declaration of Helsinki.

3.1 | Treatment regimen

An ablative fractional laser consisting of 10.400 nm CO_2 laser (CO2RE; Candela Medical) was used at 283 j/cm^2 in deep mode, medium square, single pass in the region of crow's feet and the nasolabial fold, followed by a subsequent diffuse pass in medium mode (mid-mode) at 16 J/cm^2, single pass.

Immediately after the laser, the product of study or vehicle was applied to each hemifacial area according to randomization (T0). Subsequently, the product or the vehicle was applied every 12 hours for the first week (T1-T7) and then once daily (T8-T21). Topical photoprotection was mandatory on both sides and Endocare® moisturizing cream with SCA 6% or vehicle-moisturizing cream according to randomization. Altogether, we scheduled five visits: T0 (laser session), T1d (24h), T3d (72h), T7d, and T21d.

3.2 | Clinical assessment

Clinical and adverse events were studied in all visits as well as objective parameters with micro-dermatoscopic photography Medicam® 1000 (Fotofinder systems, inc.) and transepidermal water loss (TEWL) with Tewameter® TM 300 (Courage & Khazaka electronic). Furthermore, at T0 micro-dermatoscopic photography, Tewameter and adverse event assessment were carried out before and just after laser treatment. The skin elasticity and firmness (Cutometer® dual MPA 580 (Courage & Khazaka electronic)) and the quantitative determination of wrinkle depth (Visioscan® VC 98 USB (Courage & Khazaka electronic)) and wrinkle area (VisioFace® 1000D (Courage + Khazaka electronic GmbH, Germany)) were recorded at T0 and T21.

3.2.1 | Instrumental determination

To assess efficacy, the following cutaneous biometric evaluations were performed:

Micro-dermatoscopic photography: microcolumn density evaluated with dermoscopy in semiquantitative scale (0-3): 0: absence of microcolumns; 1: slight microcolumns density; 2: moderate microcolumns density to 3: intense microcolumns density. This evaluation was assessed immediately after laser treatment: T0 and at T1d, T3d, T7d, and T21d.

Skin barrier function: quantitative determination of the transepidermal water loss (TEWL), which represents skin integrity and moisturization (high levels of TEWL is correlated with a loss in skin barrier function) at basal time (pre- and postlaser treatment (T0) and after 1, 3, 7, and 21 days.

Skin viscoelastic properties: mechanical and viscoelastic properties at basal time and after 21 days.

Anti-wrinkle efficacy: Topographic analysis of epidermis to set anti-wrinkle efficacy at T0 and T21. The wrinkle area was set at that visits.

3.2.2 | Subjective evaluations

In addition to instrumental evaluation, several clinical evaluations were performed by the investigators:

Adverse effects of intensity postlaser on each hemiface: Scale front 0 (none) to 3 (intense) regarding erythema, edema, burning

sensation, tightness, and others. It was evaluated at basal time and after 1, 3, 7, and 21 days.

Photoaging severity according to investigator on each hemiface, based on Rao-Goldman 5-point scale (RGWS): (1) without wrinkles to (5) very deep wrinkles with defined grooves. It was evaluated at all the visits.

Improvement according to investigator: IGA (−2 to 3) on each hemiface, from −2 (great worsening) to 3 (intense improvement). It was evaluated pretreatment and 21 days after laser treatment.

Improvement according to the patient: PGA (−2 to 3) on each hemiface, from −2 (great worsening) to 3 (intense improvement). It was evaluated pretreatment and 21 days after laser treatment.

3.3 | Statistical study

Ordinal variables (such as side effects or microcolumn density) were studied with the nonparametric Wilcoxon test. Quantitative variables (TEWL, elasticity, and firmness) were studied with mixed linear models (MLM) and generalized estimation equations (GEE). Mean, standard deviation, and median were calculated for all values. A statistically significant difference between hemifaces was set at $P \leq .05$.

4 | RESULTS

The 10 volunteers included in the study finished it.

One week after the ablative fractional laser treatment (T7), the postlaser microcolumn density measured by dermoscopic evaluation decreased in 90% of the patients on the side treated with the active versus 50% of the patients on the side treated with the vehicle ($P \leq .05$). The average difference in the microcolumn density decrease was 83% when comparing active- vs vehicle-treated side. This difference was statistically significant ($P = .04$). Due to swelling and erythema, differences in changes in microcolumns at T1 and T3 were difficult to measure (Figures 1, 2). At T21, there were not significant changes, probably because of complete microcolumn healing in both hemifaces, as expected.

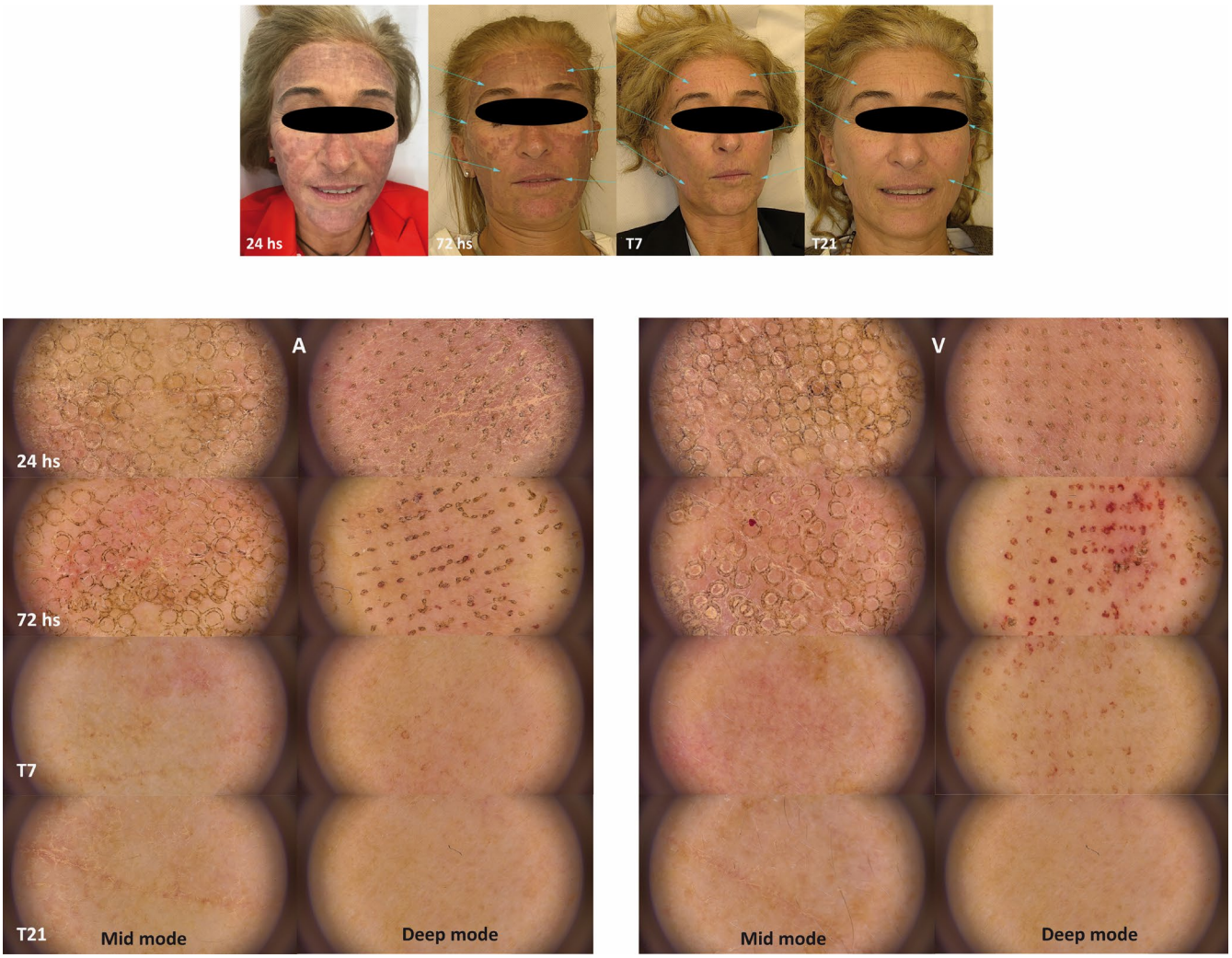

FIGURE 1 Evolution of clinical changes and microcolumn density on active-treated side (left) and vehicle-treated side (right) in volunteer #10. A (active), V (vehicle)

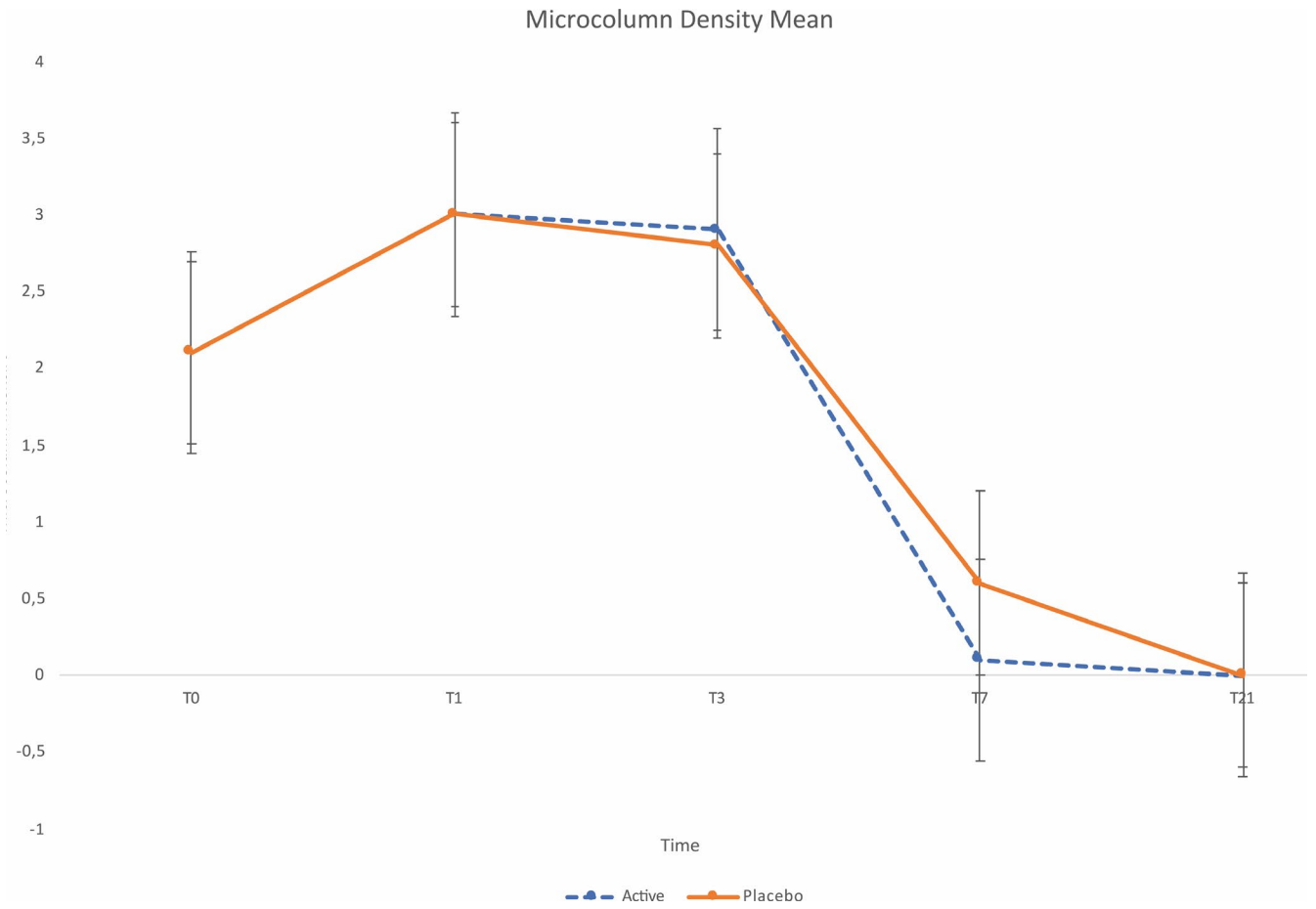

FIGURE 2 It shows that the reduction of microcolumn density after ablative fractional CO_2 laser was significantly faster on the active-treated side compared to vehicle (A: active; V: vehicle; T: time)

TABLE 1 It shows a significant better and faster improvement in barrier function and side effects on the active treated side (A) vs the vehicle treated side (V).

Evaluation	Characteristic evaluated	Improvement significantly better on active-treated side vs vehicle-treated side (p value)	Time and differences A vs V side
TEWL decreased	Barrier function	$P \leq .05$	T3, T7, T21 (Figure 3)
Erythema decreased	Side effect	$P \leq .05$	T3 (−21%), T7 (−45%), T21 (−33%)
Burning sensation	Side effect	$P \leq .001$	T3 (−32%), T7 (−59%)
Tightness	Side effect	$P \leq .05$	T3 (−24%), T7 (−53%)
Edema	Side effect	No significant	No significant difference

With respect to skin barrier function as measured by TEWL, a significant difference in reduction in TEWL was detected in favor of the active-treated side (Table 1) (Figure 3).

With respect to side effects, in Table 1 are shown a faster improvement for the active-treated side (as not in all the visits the differences were significant) (Figure 4).

A significant increase in elasticity at the end of the study (T21) with respect to basal (T0) for both hemifaces that could be attributable to laser treatment. These changes were not significant when compared active- vs vehicle-treated side. With respect to basal, no changes in firmness were assessed.

A significantly greater average wrinkle decrease was obtained on the SCA-treated side at T21 ($P \leq .05$) where wrinkle depth decreases an average of 50% in relation to the hemicara treated with the vehicle.

Compared with basal data, we obtained an improvement in Rao-Goldman scale in both hemifaces at T7, being highly marked at T21, but without significant difference between hemifaces. Both IGA and PGA detected moderate or intense improvement at T21. At that time, investigator and patients' subjective evaluation recorded no significant differences.

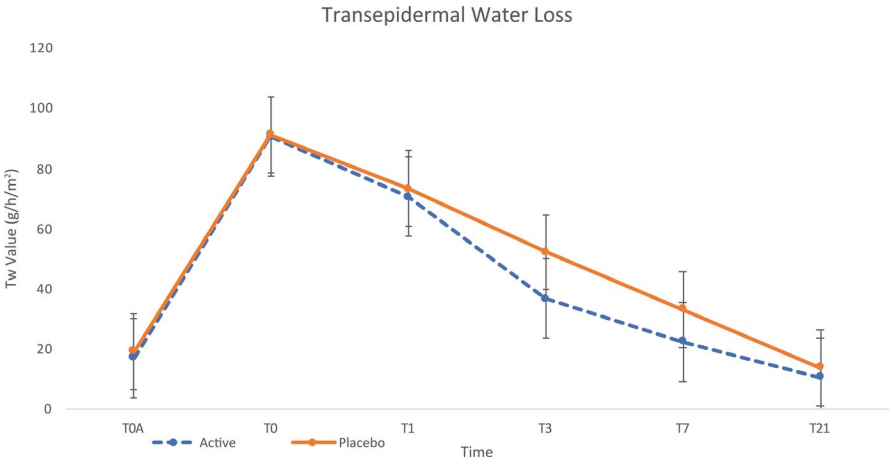

FIGURE 3 It shows the TEWL changes on the active-treated side (A) and vehicle-treated side (V), reflecting that TEWL was significantly less since T3 on the active-treated side

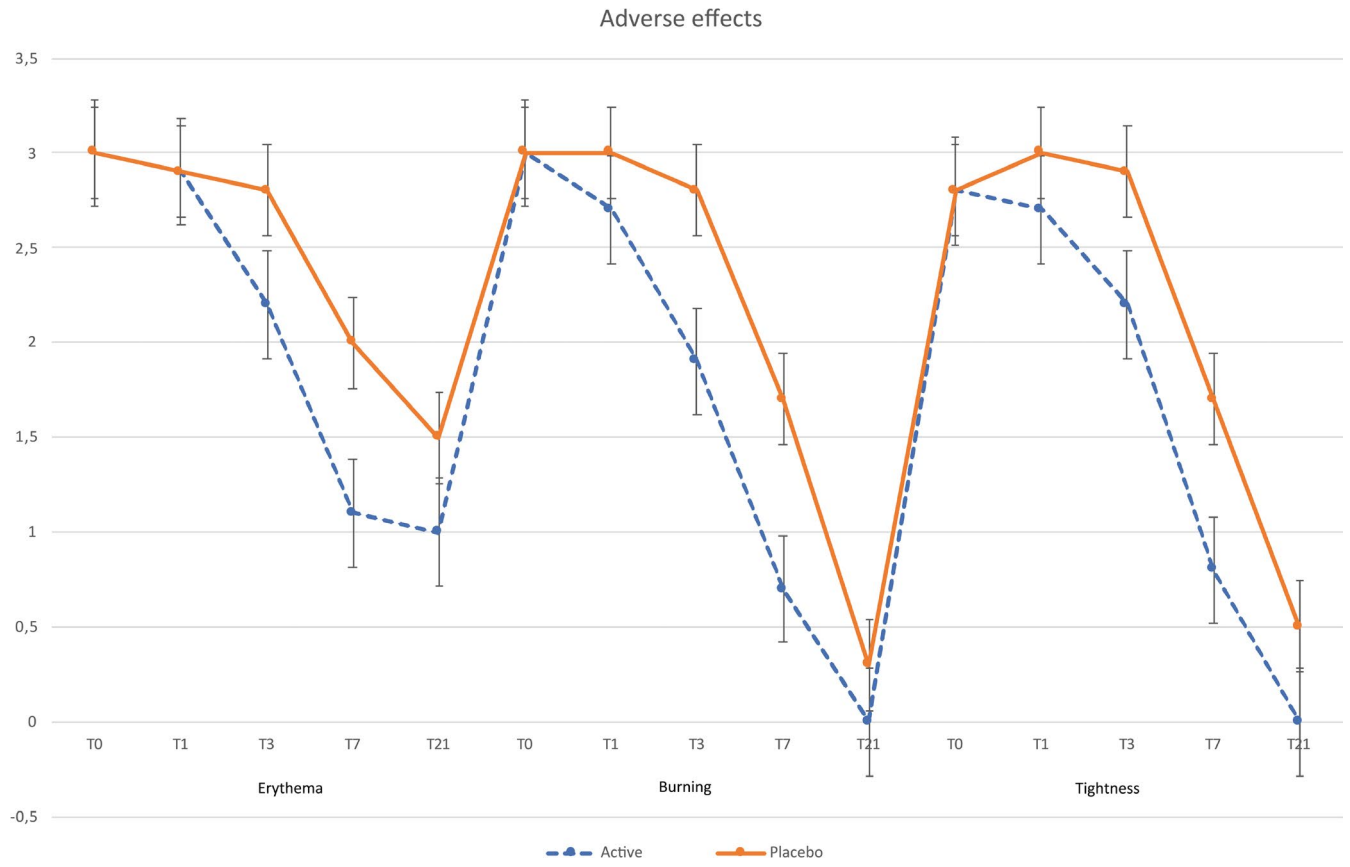

FIGURE 4 It shows significantly less side effects such as erythema, burning sensation, and tightness on the active-treated side (A) compared to the vehicle-treated side (V)

5 | DISCUSSION

Ablative fractional laser induces a controlled damage by generating cutaneous microcolumns.[11,12] In our study, the healing of the microcolumns caused by the laser treatment was faster on the SCA-treated side. The microcolumn density was 83% less perceptible in the active side compared with the vehicle side at T7 (statistically significant). This means that SCA can induce faster healing of the microcolumns caused by the fractionated ablative laser. This was previously described after nonablative fractional laser.[13]

Skin integrity and barrier function improvement were significantly greater just 72 hours after laser treatment on the SCA-treated side. This difference was maintained at T7 (7 days postlaser) and at T21 (21 days postlaser).

These findings support many previous in vitro and clinical studies that demonstrated the potential of SCA to induce fibroblast and

keratinocytes migration, increasing wound healing through improving cellular structures and extracellular matrix formation.[8-10] Thus, the fact that SCA is able to regenerate the microcolumns faster is directly related to the faster improvement in skin integrity and barrier function.

With respect to adverse effects resulting from the procedure, we found a significant faster fading of erythema, burning, and dryness on the SCA-treated side beginning at T3 (72 hours post-laser). A product that reduces these adverse effects implies faster healing and greater procedure tolerability and adherence by patients. In our study, there were not significative differences in edema changes. This may be a consequence of the prompt disappear of this effect, which is difficult to measure once the procedure has been performed.

No significant differences in firmness were detected with respect to baseline in none hemiface. On the other hand, an improvement in elasticity was detected at the end of the study in both hemifaces but with no significant difference between the two sides. We hypothesize that enhancement on the vehicle-treated side treated was determined by the changes induced by ablative fractionated laser. Changes in firmness might have been detected at a later date (2 or 3 months after laser) due to the delayed effect of fibroblast stimulation and skin remodeling.

After 21 days, the wrinkle depth reduction of the skin on the SCA-treated side compared to vehicle-treated side was significantly higher (average 50%; $P \leq .05$). We hypothesize that a synergic effect between CO2 laser and SCA treatment would be responsible of this fast improvement in clinical wrinkles. These results are consistent with the hypothesis that GAGs and growth factors of SCA secretion induce dermal stimulation that leads to improvement in wrinkles.[8-10,13]

The main limitation of this study is its small sample size for a controlled clinical trial.

In conclusion, we obtained a significant faster improvement with a significant decrease in the microcolumns created by the laser on the hemiface that received after laser, the application of SCA 40% and a moisturizing cream with SCA 6%. Common adverse effects (erythema, burning, and tightness) are also significantly reduced, increasing procedure tolerance and adherence to the treatment. Furthermore, a significant improvement in wrinkles after laser treatment was seen in the SCA-treated area.

CONFLICT OF INTEREST

Dra Truchuelo is scientific adviser to Cantabria laboratories.

DATA AVAILABILITY STATEMENT

It encourages data sharing.

ORCID

M. Teresa Truchuelo https://orcid.org/0000-0002-9691-0476

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