Creating the Optimal Environment for Managing Treatment-Induced Skin Breakdown: Clinical and Laboratory Evaluations

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Hyaluronic acid is a natural part of the extracellular matrix of the skin. When applied topically, it has been reported to create an optimal environment for healing. We studied the efficacy of hyaluronic acid sodium salt 0.2% gel in reducing the typical cutaneous side effects of intense pulsed light, namely erythema, peeling, scabbing, and, rarely, blistering, for the treatment of photodamaged or photoaged skin. Ten healthy female subjects (aged 46–67 years) with photodamaged or photoaged skin who had previously been treated with intense pulsed light were enrolled. The study was institutional review board–approved and all subjects signed an informed-consent release. This clinical study design was a 2-week, double-blind, split-face, randomized prospective trial. Subjects applied the hyaluronic acid sodium salt 0.2% gel and comparable vehicle to the designated treatment area (right or left side of face) twice a day for 2 weeks. All subjects were evaluated and clinically graded at visit days 1 (baseline), 4, 7, and 14 with digital photography and cross-polarized photography. Out of the 10 subjects, 6 subjects were observed with optical coherence tomography, 7 subjects with transepidermal water loss, and 7 subjects with capacitance (all performed at baseline and days 4, 7, and 14). All of the patients showed smoother skin with improved texture. Erythema was decreased for many patients on the side treated with hyaluronic acid sodium salt 0.2% gel at some visits during the study. Hyaluronic acid sodium salt 0.2% gel was found to be effective and safe in these subjects.

The StarLux® Pulsed Light and Laser System with the LuxG™ handpiece is designed to effectively treat facial telangiectasia and other vascular lesions, as well as benign pigmented lesions. By configuring the proper wavelength range and fluence, as well as surface cooling, one can selectively target vascular and pigmented lesions. The size of the intense pulsed light (IPL) head on the LuxG handpiece is 10×15 mm, and the handpiece uses 1- to 5-millisecond pulses with a range of wavelengths (500–670 nm and 870–1400 nm) so that both vessels and pigmented lesions can be selectively targeted. The StarLux system uses direct cooling with a sapphire tip that is held in contact with the skin.

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STUDY TREATMENTS

All subjects underwent the same IPL treatment of the entire face and then applied hyaluronic acid sodium salt 0.2% gel (active) on one half of the face and a comparable vehicle gel (control) on the other half of the face.

INSTRUCTIONS FOR USE AND ADMINISTRATION

Patients were to cleanse the entire face twice daily with a gentle liquid cleanser, pat dry, and then apply the appropriate formulation (hyaluronic acid sodium salt 0.2% gel or the comparable vehicle) to the specified half of the face. Subjects were instructed to avoid excessive sun exposure (ie, sunlight, tanning booths) and were instructed to wear protective clothing when they went out into the sun (eg, large-brimmed hats).

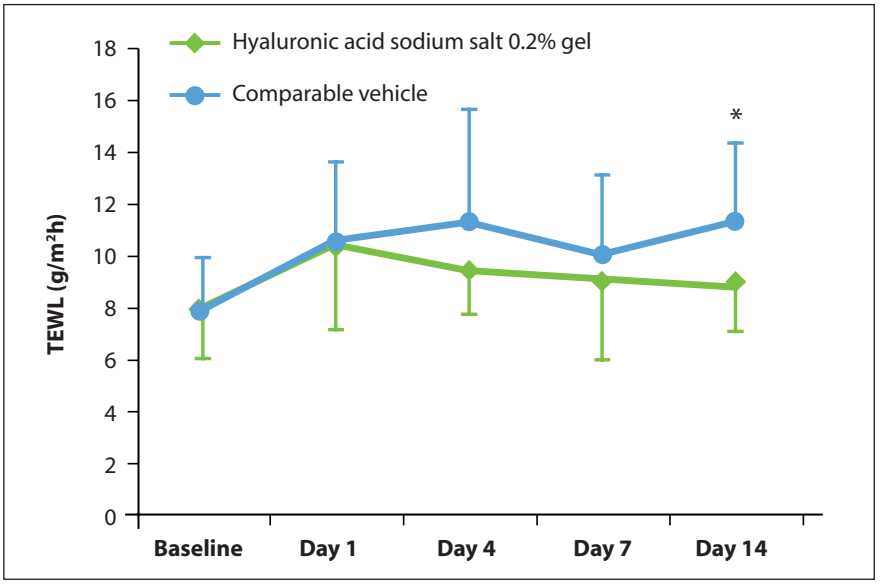

Figure 1. Transepidermal water loss (TEWL) in patients treated with hyaluronic acid sodium salt 0.2% gel and comparable vehicle. Asterisk indicates statistically significant difference (P=.019).

NONINVASIVE MEASUREMENTS

Barrier function of the skin was assessed by measuring the transepidermal water loss (TEWL) with an evaporimeter.[1] Measurements were done in an environmental chamber (temperature, 70±0.5°F; relative humidity, 40±5%). The data were collected through the DermaLab® TEWL device for 1 minute and the average of the last 8 readings were taken for the value in g/m²h.

A corneometer measures the level of hydration in the stratum corneum.[2] Measurements were done with a pair of electrodes formed as an interdigital grid with small spacing between the 2 electrodes. The moisture content of the stratum corneum was given in relative units. Measurements were done in an environmental chamber (temperature, 70±0.5°F; relative humidity, 40±5%). After at least 15 minutes of acclimation, the probe was placed on the subject's skin, pressing the spring-loaded system. The instrument recorded the reading in 1-second intervals.

Optical coherence tomography (OCT) is a new technique to record skin structures in depth.[3] OCT images skin as vertical sections with resolutions reaching 3 µm in lateral direction and 5 µm in depth. OCT is based on an optical interferometry principle in which a broadband light beam of short-coherence wavelength is split into sample and reference beams; the reflected light is coupled to produce an interference signal. Dermal and epidermal structures are clearly outlined. The stratum corneum is visualized as a bright band and its thickness can be estimated. The geometry of isolated legions, such as comedones, can also be visualized.

Digital photographs were taken with a digital camera equipped with a Canfield polarized flash system; one linear polarizer filter was placed in front of the flash and another was placed in front of the camera lens. The 2 filters were then rotated in perpendicular or parallel positions to achieve cross-polarization or parallel polarization, respectively. Parallel photography enhances visualization of the depth of wrinkles whereas cross-polarization enhances the visualization of red (vascular) and brown (lentigines) pigmentation.

Clinical evaluations were conducted by a dermatologist on days 1, 4, 7, and 14. Evaluations were graded using 4-point scales to assess erythema (0=none; 1=minimal—scant, rare erythema; 2=mild—pink coloration in some of the treatment area; 3=moderate—bright red color involving some of the treatment area, or pink color involving all of the treatment area; and 4=severe—areas of fiery red coloration or bright red coloration of all of the treatment area) and oozing or crusting (0=none; 1=minimal—a single area of oozing or crusting ≤3 mm; 2=mild—more than a single area of oozing or crusting ≤3 mm; 3=moderate—1 or more areas of oozing and crusting ≥3 mm in size; and 4=severe—confluent areas of oozing or crusting).

PATIENT EVALUATION QUESTIONNAIRES

All patients completed a questionnaire designed to allow for their assessment at each clinical evaluation by the dermatologist.

RESULTS

Transepidermal Water Loss

At day 14, the active side showed a statistically significantly lower TEWL value than the control side

(8.71 g/m²h vs 11.24 g/m²h; $P=.019$, using a 2-tailed *t* test) (Figure 1).

Corneometer

Hydration measured by the corneometer did not show a statistical difference between the active and control sides.

Optical Coherence Tomography

A total of 300 images were collected from 6 subjects. Many images showed no clear-cut differences between the active and control sides; however, some subjects' images did show differences. In these cases the active side had brighter as well as more uniform morphology in the papillary and upper reticular dermis (Figure 2). Particularly on days 4 and 7, several subjects showed slight differences between the active and control sides.

Photography

Photographs of all subjects showed that the skin had a more even tone (Figures 3 and 4). In a self-assessment questionnaire, the subjects stated that their skin was smoother and had an improved texture.

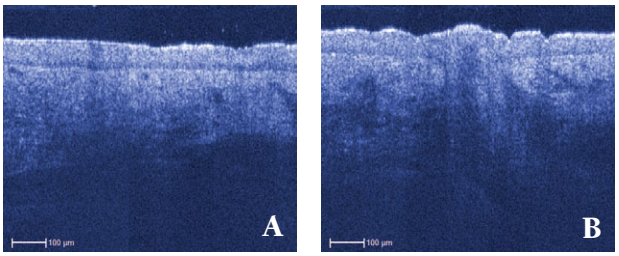

Figure 2. Optical coherence tomography at day 14 in patients treated with hyaluronic acid sodium salt 0.2% gel (A) and comparable vehicle (B).

CLINICAL AND SUBJECTIVE EVALUATIONS

All subjects thought that both products were easy to apply, soothing, spread easily, made skin feel smooth, and did not interfere with make-up application after use. Compared with their previous IPL treatments, the majority of subjects felt that, on the active side of the face, the

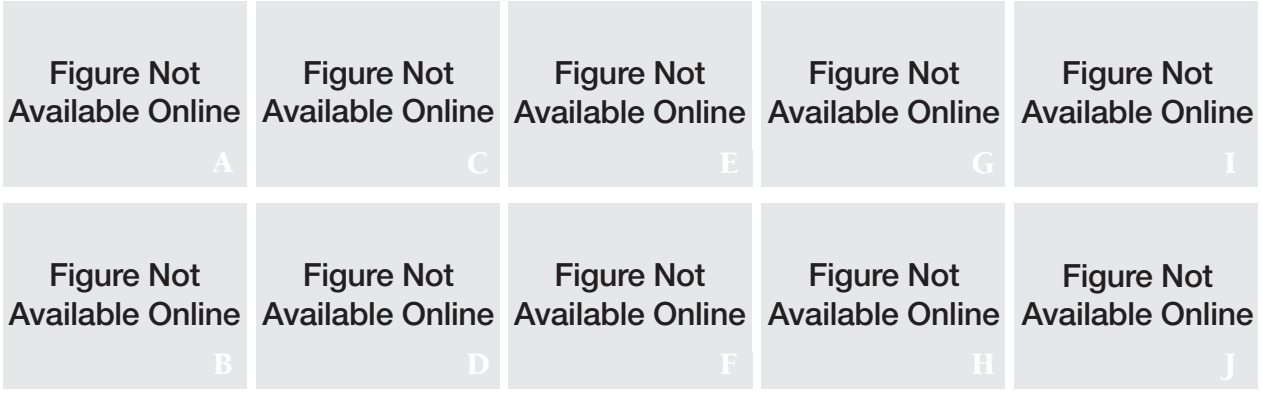

Figure 3. Cross-polarized digital photographs taken at baseline (A, B) and days 1 (C, D), 4 (E, F), 7 (G, H), and 14 (I, J) showed erythema subsided faster on the left side of the face, treated with hyaluronic acid sodium salt 0.2% gel, compared with the right side, treated with comparable vehicle. There were no breakouts. The skin on the left side of the face was smoother and had improved texture from baseline.

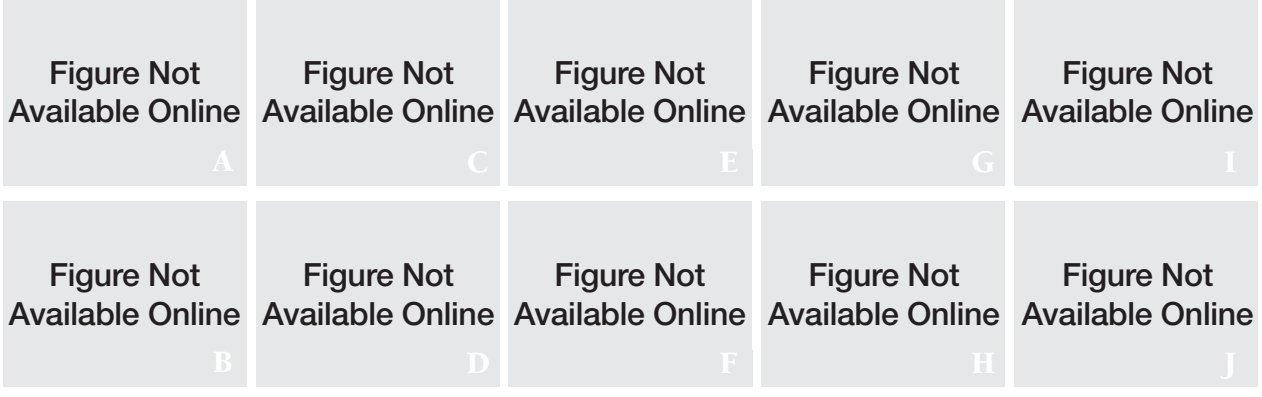

Figure 4. Standard digital photographs taken at baseline (A, B) and days 1 (C, D), 4 (E, F), 7 (G, H), and 14 (I, J) showed erythema subsided faster on the left side of the face, treated with hyaluronic acid sodium salt 0.2% gel, compared with the right side, treated with comparable vehicle. There were no breakouts. The skin on the left side of the face was smoother and had improved texture from baseline.

side effects of the IPL treatment subsided faster and were not as severe as those on the side of the face treated with the control vehicle. The redness subsided faster on the active side of the face than on the control side, and the overall discomfort was diminished after use of both the active and the control products. Many of the subjects showed less erythema on the active side compared with the control side. The active side of the face showed a trend toward greater improvement.

SUMMARY AND DISCUSSION

Hyaluronic acid sodium salt 0.2% gel helped manage typical cutaneous side effects of IPL treatment for photodamaged or photoaged skin. Hyaluronic acid sodium salt 0.2% gel was well tolerated with no breakouts. Noninvasive bioengineering measurements and standardized photography confirmed clinical changes observed, which included improved TEWL with the active-treated side, indicating improved barrier properties of the horny layer, and coherent epidermis as observed by OCT.[4,5] Hyaluronic acid may enhance healing because it is a natural part of the extracellular matrix of the skin and has humectant properties. In addition, hyaluronic acid appears to block the cyclooxygenase-2 pathway (J. Folkman, oral communication, June 2002). Therefore, by interfering with the inflammatory pathway, one may expect hyaluronic acid to minimize erythema.[6] The active material was clearly beneficial, as is evident from the various bioengineering measurements that were performed.

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