Skin Rejuvenation with Intense Pulsed Light

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SUMMARY Skin rejuvenation has developed into one of the most popular indications for laser and intense pulsed light (IPL) treatment in dermatology. During the past few years, nonablative skin rejuvenation with infrared lasers has become ever more popular. The results for hyperpigmentation, telangiectasias and erythema are very good, whereas the results in treating wrinkles are not as good as with ablative therapy.

KEY WORDS: skin rejuvenation, intense pulse laser

INTRODUCTION

Skin rejuvenation has developed into one of the most popular indications for laser and intense pulsed light (IPL) treatment in dermatology.

Type I damage includes hyperpigmentations, telangiectasias and erythemas, while type II damage refers to wrinkling (1). Over 15 years ago, pulsed and scanned ablative lasers such as CO_2 or Erbium:YAG were introduced for the treatment of ablative skin rejuvenation. Although excellent results can be obtained with these lasers, the high risk of scarring and the long downtime after the procedure present major disadvantages.

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Rejuvenation with IPLs

Bjerring *et al*. compared different filter combinations of IPL (Ellipse Flex) in patients with sun-damaged type I skin. Patients with ectatic blood vessels were treated with the pulse duration of 15 to 30 ms and energy density of 14 to 15 J/cm². Hyperpigmentations and diffuse erythemas were treated with double pulses of 2 ms at 10-ms intervals. The energy dose was 8 to 10 J/cm². Telangiectasias and erythemas responded best to the filter combination of 530 to 750 nm, and hyperpigmentations to the combination of 555 to 950 nm. Acute side effects were edemas and erythemas; scarring and atrophy were not observed (1).

Jorgensen *et al*. (2) evaluated the efficacy and adverse affects of long-pulsed dye lasers (LPDL) *versus* IPL-therapy for the treatment of photodamaged skin in 20 women. In this study, LPDL rejuvenation resulted in better vessel clearance and

less pain. Disturbances of pigmentation and skin texture improved with both modalities without any significant side-to-side differences. Reduction of rhytids could not be seen with either of the two techniques.

Hedelund *et al.* (3) treated 32 women with an IPL (Ellipse Flex). Nine months after the final treatment, blinded investigators and patients reported significant improvements between treated and untreated telangiectasias and irregular pigmentations, but no significant difference between treated and untreated rhytids.

In a split-face study, Kono *et al.* (4) compared the efficacy of IPLs *versus* long-pulsed dye lasers in Asian patients. Three months after the last treatment, lentigines had improved in the IPL-treated area by 62% compared to 81% in the other area. No significant difference in wrinkle reduction could be observed between IPL-treated and LPDL-treated areas.

Erythrosis interfollicularis is a specific form of sun-induced skin damage that presents mainly at the side of the neck and the décolleté area. Wenzel *et al.* (5) have reported successful treatments with an IPL device and clearance rates of 75% to 90%.

In summary, IPL treatment represents a good alternative to laser therapy for type I-damaged skin (telangiectasias and hyperpigmentation) (Figs. 1-3) (6).

Rejuvenation with PDT

In search for the new possibilities of skin rejuvenation, topical photodynamic therapy (PDT) is increasingly applied with various light sources. PDT with 5-aminolevulinic acid (ALA) in combination with blue light was approved by the Food and Drug Administrations (FDA) for the treatment of

actic keratoses (AK) in 1999. It has become clear that PDT provides a potential tool for skin rejuvenation besides the treatment of non-melanoma skin cancer. PDT requires a photosensitizer localized in the target tissue and irradiation with visible light. For topical PDT, ALA is applied either as a cream base or as a solution (Levulan® Kerastick®, DUSA Pharmaceuticals, Inc., Wilmington, MA) as well as its methylester derivative (methylaminolevulinate, MAL) (Metvix® (Metvixia® in France and U.S.), Galderma, France). Modified enzyme activities in tumor cells and increased uptake in altered keratinocytes maintain the accumulation of the endogenous photosensitizer protoporphyrin IX. Activation by light of the appropriate wavelength leads to the generation of singlet oxygen or reactive oxygen species, resulting in selective destruction of photosensitized cells. Broadband IPL is suitable for the activation of protoporphyrin IX because of its absorption bands at 410, 504, 538, 576 and 630 nm.

Most studies on photodynamic photorejuvenation, a term describing the reversal of the signs of photodamage, have been conducted with IPL devices. Three prospective, randomized split-face trials with 20% ALA as a photosensitizer for photodynamic rejuvenation have been conducted so far (7-9). These studies show that the adjunctive use of ALA is more beneficial in the treatment of photodamaged skin than IPL treatment alone.

One prospective, randomized, single-blinded, IPL split-face trial was conducted by Dover *et al.* (8), who included 20 patients receiving 5 treatments in 3-week intervals. ALA solution (Levulan® Kerastick®, DUSA Pharmaceuticals, Inc., Wilmington, MA) was applied on one half of the face 30 to 60 min prior to the first three IPL-treatments;

Figure 1. Telangiectasias on the cheeks and nose of a patient aged 45 before treatment.

Figure 2. Significant improvement of telangiectasias in the treatment area 6 weeks after the first treatment with IPL (Ellipse Flex, 555 nm, 13.2 J/cm², two pulses).

analysis (10). Seven patients with mild facial photodamage received two full face IPL treatments in a 1-month interval. A 560 nm cut-off filter was used to deliver light with 27 to 30 J/cm² using a double pulse of 2.4 and 4 ms and a 10 ms delay between pulses. Punch biopsies, made prior to the treatment and three months after the last treatment, showed increased type I collagen in the dermis, which was evident especially in the ALA-IPL group. A subjective advancement of skin quality was found in all seven patients, whereas the observed side effects were minimal.

A retrospective study of 17 patients evaluated the efficacy of ALA-PDT using IPL in the treatment of AKs and signs of photoaging (11). After an incubation time of 1 hour, IPL was used with a 560 nm filter at 28 to 32 J/cm² with a double pulse of 3.0 ms and 6.0 ms and a delay of 10 ms. Besides the healing up of 68% of AKs, a 48% improvement in pigmentary irregularities and 25% improvement in coarseness of the skin texture were monitored, but there was no change in fine wrinkle appearance.

The mode of action of rejuvenation with IPL-PDT is not yet completely understood. As a consequence of an up-regulated ALA uptake and modified enzyme activities, PpIX accumulates in altered keratinocytes. Thus, selective destruction of those keratinocytes through PDT results in rapid healing (12). The epidermal renewal due to exfoliative effects and epidermal proliferation improves the skin texture and leads to less roughness, increased epidermal thickness and less pigmentary changes. Moreover, neocollagenesis as an indirect dermal effect of IPL-PDT is stimulated by cytokine induction (10,13,14). Cytokines derived from epidermal keratinocytes penetrate the basal layer and trigger matrix metalloproteinase (MMP) production in dermal fibroblasts. The accumulation of partially degraded and fragmented collagen, as present in photoaged skin, inhibits neocollagenesis (15). Thus, proteolytic clearance of accumulated fragmented dermal collagen by MMPs plays a decisive role in restoring collagen biosynthesis (16-18).

Figure 3. Considerable improvement of telangiectasias on the cheeks and nose after three treatment sessions (Ellipse Flex, 555 nm, 13.2 J/cm², 30 pulses in four-week intervals).

the last two treatments consisted of IPL treatment only. The ALA-IPL group showed better results for the global score for photoaging (80% *vs*. 45%; *P*=0.008), improvement of fine lines (60% *vs*. 25%; *P*=0.008) and mottled pigmentation (85% *vs*. 20%; *P*<0.001). The final cosmetic evaluation by the investigator and patient satisfaction scores was significantly higher than that for the IPL-only sides. Pretreatment with ALA did not enhance the efficacy on sallowness and tactile roughness. The incidence of adverse effects was higher on the ALA-IPL sides, and patients experienced more intense erythema (50% *vs*. 15%; *P*=0.04), scaling and dryness (50% *vs*. 15%; *P*=0.04), edema (50% *vs*. 10%; *P*=0.01) as well as crusting and vesiculation (20% *vs*. 5%; *P*=0.11).

Another trial was conducted to compare short-contact ALA-PDT to IPL alone for enhancing diffuse photodamage (9). Patients (n=16) received three treatments in 1-month intervals. With respect to all treatment parameters (crow's feet, telangiectasias, mottled hyperpigmentation and tactile skin roughness), considerably better improvements were found on the sides treated with PDT.

Marmur *et al*. conducted a split-face study to investigate changes in collagen formation after ALA-PDT by electron microscopic ultrastructural

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