Efficacy of IPL device combined with intralesional corticosteroid injection for the treatment of keloids and hypertrophic scars with regards to the recovery of skin barrier function: A pilot study

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Abstract

Background: Keloids and hypertrophic scars are prevalent and psychologically distressful dermatologic conditions. Various treatment modalities have been tried but without complete success by any one method. Objective: We evaluated the efficacy of a combination of intense pulsed light (IPL) device and intralesional corticosteroid injection for the treatment of keloids and hypertrophic scars with respect to the recovery of skin barrier function. Methods: Totally 52 Korean patients were treated by the combined treatment at 4–8-week intervals. Using digital photographs, changes in scar appearance were assessed with modified Vancouver Scar Scale (MVSS), physicians’ global assessment (PGA) and patient’s satisfaction score. In 12 patients, the stratum corneum (SC) barrier function was assessed by measuring transepidermal water loss (TEWL) and SC capacitance. Results: Most scars demonstrated significant clinical improvement in MVSS, PGA and patient’s satisfaction score after the combined therapy. A significant decrease of TEWL and elevation of SC capacitance were also documented after the treatment. Conclusion: The combination therapy (IPL + corticosteroid injection) not only improves the appearance of keloids and hypertrophic scars but also increases the recovery level of skin hydration status in terms of the skin barrier function.

Introduction

Keloids and hypertrophic scars occur as a result of excessive fibroblast proliferation and accelerated collagen synthesis with an abnormal wound healing process that have a prolonged phase of inflammation and fibroplasias (1,2). Clinically, they are present as erythematous to purplish, well-demarcated, firm, elevated papules and plaques often associated with subjective symptoms, such as pruritus and pain.

These scars are prevalent and both cosmetically and psychologically disturbing to many patients and challenging for dermatologists; whatever their origins (post-traumatic, surgical and/or idiopathic scar) are; and wherever their locations (anterior chest, shoulder, face and anywhere in the body) are. The accurate pathogenesis of these scars has been unknown, so treatment for these conditions became more complicated. Various treatment modalities including topical and intralesional steroids, cryotherapy, radiation, surgical excision and pressure dressings have been tried but without complete success by any one method (3–6).

Intense pulsed light (IPL) has been widely used for photo rejuvenation and to treat a variety of vascular lesions and pigmented lesions (7–10). Its effect on keloids and hypertrophic scars has been previously examined (4,5,11,12). Combination of IPL along with intralesional corticosteroid injection was relatively effective in treating keloids and hypertrophic scars (13).

With regards to skin barrier function, particularly skin hydration status, decreased water content and increased transepidermal water loss (TEWL) in keloids and hypertrophic scars were already documented (14). However, there has been no report on the changes of skin hydration status of keloids and hypertrophic scars before and after IPL treatment alone or combination therapy.

The objective of this pilot study is to evaluate the efficacy of a combination of IPL device and intralesional corticosteroid injection for the treatment of keloids and hypertrophic scars with respect to the recovery of skin barrier function.

Materials and methods

Patient population

The patients with keloids or hypertrophic scars, who visit our outpatient clinic of department of dermatology during the period from January 2012 to October 2014, were included in the study. The causes of the scarring were various in the patients: post-traumatic scars in 9 patients, surgical scars in 20 patients, acne scars in 10 patients and scars with no obvious predisposing cause in 13 patients. Exclusion criteria were pregnancy, breast-feeding, active local or systemic infection, hypersensitivity to light, diseases or genetic conditions causing photosensitivity or tending
to aggravate after light exposure, use of photosensitizing drugs or immunosuppressive medications, a history of malignant skin cancer and a treatment history of any other scar treatment within 3 months of entering the study.

In total, 52 Korean patients (32 women, 20 men; mean ± SD age 38.3 ± 17.9 years, range 8–77) with Fitzpatrick skin types III or IV were enrolled in the study. The study was performed in accordance with the ethical guidelines of the Declaration of Helsinki (1975), and was approved by the Institutional Review Board of Seoul National University Boramae Hospital.

Treatment protocols

Each patient was treated with a combination of IPL device (Ellipse I²PL; Danish Dermatologic Development, Hørsholm, Denmark; λem = 530–750 nm) followed by high-dose corticosteroid (triamcinolone acetonide 10–40 mg/ml) intralesional injection. Before each treatment session, standardized photographs were taken using a digital camera (EOS 500D; Canon, Tokyo, Japan). All patients received combined treatment at 4–8-week intervals; total five sessions of treatment for every patient were successfully completed.

No topical or local anesthetic was used through the treatment. Chilled colorless gel was applied directly to the assigned region immediately prior to the IPL treatment to protect the epidermis from thermal injury and to assist delivering the light uniformly to the surface of the skin. Energy density of IPL device varied from 2.5–5 ms; pulse delays of 10–20 ms and from two to four passes over the treatment area. The end point of the treatment was slight erythema of the skin surface. Following the IPL treatment, the patients were injected with triamcinolone acetonide (TA) at a dose of 10–40 mg/ml using a 31-gauge needle into the mid- and lower-dermis of keloids and hypertrophic scars. After completing combination therapy, patients were required to apply an ice pack in the treated areas for 20 min.

Efficacy evaluation by investigators

Modified Vancouver Scar Scale (MVSS) was used to provide on overall impression of the quality of the scars (15) (range = 0–18 points, Table 1). Average MVSS was calculated by dividing the sum of each component of MVSS to the number of patients. We evaluated MVSS and average MVSS for every visit including baseline MVSS. In addition, Physicians’ global assessment (PGA) was assessed 4–8 weeks after completion of five treatment sessions. Evaluations were done by grading the digital photographs of the scars by two independent physician assessors using a standard quartile grading scale (0: no satisfaction, 1: minimal, poor (less than 25%), 2: moderate, fair (25–50%), 3: good (51–75%) and 4: excellent (76–100%).

Patient’s evaluation

During every visit, possible adverse effects (e.g. purpura, hyperpigmentation and blister formation) as well as any significant changes that had occurred (e.g. decreased subjective symptoms of pain and pruritus, changes in texture, hardness and level of the skin surface) were recorded in the patients’ electronic medical records. After completion of five sessions of combination therapy, patient’s overall satisfaction score was also evaluated; 0: no satisfaction, 1: minimal, poor (less than 25%), 2: moderate, fair (25–50%), 3: good (51–75%) and 4: excellent (76–100%).

Non-invasive instrumental measurements

For more objective assessment of changes in stratum corneum (SC) barrier function, we measured TEWL (Tewameter® TM300; Courage & Khazaka Electronic GmbH, Cologne, Germany) and hydration state of SC measuring SC capacitance (Corneometer® CM825; Courage & Khazaka Electronic GmbH, Cologne, Germany) from a marked scar in 12 subjects. Each site was measured at least 10 times and the mean values were calculated.

Statistical analysis

Data analysis was conducted using SPSS® software version 19.0 for Windows (SPSS Inc., Chicago, IL). Repeated Measures ANOVA was used for data analysis. p Values of <0.05 were considered statistically significant.

Results

Investigator assessments

The average MVSS had decreased significantly after the sequential combined treatments (p <0.05) (Supplementary Figure 1). Substantial portion of the patients (37 of 52; 71.2%) achieved more than 50% of overall improvement, with PGA score higher than or equal to 2; 28.8% of patients developed more than 75% of improvement with PGA score 3 (Table 2). Representative cases

Table 1. The modified Vancouver Scar Scale (MVSS).

| Parameter   | Description                          | Score |
|-------------|--------------------------------------|-------|
| Pigmentation| Normal                               | 0     |
|             | Hypopigmentation                      | 1     |
|             | Mixed                                | 2     |
|             | Hyperpigmented                       | 3     |
| Pliability  | Normal                               | 0     |
|             | Supple (flexible with minimal resistance) | 1     |
|             | Yielding (giving way to pressure)     | 2     |
|             | Firm (inflexible, not easily moved, resistant to manual pressure) | 3     |
| Vascularity | Normal                               | 0     |
|             | Pink                                 | 1     |
|             | Red                                  | 2     |
|             | Purple                               | 3     |
| Pain        | None                                 | 0     |
|             | Occasional                           | 1     |
|             | Requiring medication                 | 2     |
| Pruritus    | None                                 | 0     |
|             | Occasional                           | 1     |
|             | Requiring medication                 | 2     |

Table 2. Physicians’ global assessment (PGA).

| Average PGA | Number of patients (%) |
|-------------|------------------------|
| 0           | 3 (5.8)                |
| 0.5         | 0 (0)                  |
| 1           | 7 (13.5)               |
| 1.5         | 4 (7.7)                |
| 2           | 18 (34.6)              |
| 2.5         | 5 (9.6)                |
| 3           | 15 (28.8)              |

PGA: 0: <25%, 1: 25–50%, 2: 51–75% and 3: >75% improvement. Average PGA = the sum of PGA score evaluated by two physicians/2.
that showed a definite response to the combined therapy are exhibited in Supplementary Figures 2 and 3.

**Patient self-assessment**

After serial combined treatments with IPL and TA injection, almost 55.8% of patients rated their results as ‘‘excellent’’ or ‘‘good’’ improvement; and 42.3% of patients estimated their results as ‘‘moderate’’ or ‘‘fair’’. No one expressed discontent or dissatisfaction with the final results (Table 3).

**Non-invasive instrumental measurements**

The mean baseline TEWL and SC capacitance were 28.7 and 35.4, respectively. Compared with the pre-treatment values, there was a statistically significant decrease of mean TEWL (p < 0.05). In addition, distinct recovery of SC capacitance to normal range was also documented (p < 0.05) (Supplementary Figure 4).

**Adverse effects**

There was no serious adverse effect during the combined treatment. Most patients experienced transient erythema and tolerable pain, which disappeared within a few minutes after applying an ice pack. Slight depression around treated areas was documented in three subjects, however all adverse effects were resolved within several weeks without any permanent discomfort.

**Discussion**

Treatment of keloids and hypertrophic scars using a combined therapy of IPL followed by TA injections showed both significant clinical improvement and recovery of skin hydration status.

Theoretically, IPL is designed to emit wavelengths from visible light to infrared light. By means of convertible cut-off filters, IPL can be used to target melanin, hemoglobin and/or water selectively as the primary chromophores, while protecting the surrounding tissue (11,16). Previous studies reported the successful outcome and the efficacy of IPL treatment for keloids and hypertrophic scars suggesting diverse theories and mechanisms of IPL through selective photothermolysis (13,17–19). IPL has effectively treated various kinds of vascular and pigmented lesions through selective targeting of hemoglobin and melanin. In addition, IPL is postulated to improve clinical appearance of keloids and hypertrophic scars by a mechanism similar to pulsed dye laser (PDL) by: targeting neovascularization essential to the collagen overgrowth; causing tissue hypoxia and changing production of extracellular matrix components and modifying collagen synthesis of fibroblast and collagen degradation with secretion of metalloproteinase (19–23). Moreover, in the case of combined treatment protocol (IPL with TA injection), the important benefits gained from IPL was the reduction of telangiectasia, which is sometimes easily induced by the repetitive intraleisional TA injections, and therefore resulted in a cosmetically acceptable outcomes of the scar (24). According to Weiss et al., IPL can affect significant improvement in hypertrophic scars comparable with the gold standard PDL, and offers a therapeutic alternative to PDL since it minimizes the development of post-treatment purpura (19). Furthermore, McGill et al. reported that IPL can affect deeply located vessels and dermal components, because IPL includes relatively long wave length and large-sized tip (25). Large-sized tip also helps to reduce treatment time, and IPL is more cost-effective therapy than PDL. These properties of IPL can be the strength for treating keloids and hypertrophic scars.

On the other hand, intraleisional corticosteroid injections have become a mainstream in the treatment of keloids and hypertrophic scars, alone or in combination with other therapeutic modalities, such as laser and cryotherapy (1–4,26). TA injection can flatten and soften scars, but cannot narrow or completely eliminate them (27). Intralesional TA injection into mid- or lower-dermis decreases fibroblast proliferation, collagen synthesis and glycosaminoglycan synthesis and suppresses pro-inflammatory cytokines and mediators (28), so it has been used as an important treatment option for keloids and hypertrophic scars.

With respect to the skin hydration status, in a previous study on functional analyses of the SC in scars, both TEWL and high-frequency conductance remained high in hypertrophic scars and keloids (14,29). Moreover, in hypertrophic scars and keloids, the SC functional aberrations lasted for an extended period, probably reflecting the sustained inflammatory changes that take place in the dermis. In the same context, the recovery of those altered barrier function of the SC as assessed by TEWL is a relatively reliable parameter (14,29). In comparison with the normal value of TEWL (8–14 g/h/m²) and SC capacitance (more than 40 a.u.), our study subjects showed high TEWL (28.7 ± 6.5; mean ± standard error of the mean) and low measured value of SC capacitance (35.4 ± 3.5) before treatment. After completion of five treatment sessions, significantly decreased TEWL (9.4 ± 1.2, p < 0.05 versus baseline) and recovery of SC capacitance to normal healthy range (45.2 ± 2.1, p < 0.05 versus baseline) were documented in all patients. Berman et al. reported that the clinical efficacy of increased hydration for blanching and flattening of hypertrophic and keloid scars may make improvement of subjective symptoms as well as recovery of pliability (30). As mentioned above, because IPL includes relatively long wave lengths and large spot size, it can induce deeper dermal changes in vessels and collagens: modifying dermal collagen synthesis and degeneration; transmuting production of extracellular matrix and secretion of various cytokines. Those dermal changes stimulated by intradermal TA injection may closely interact with epidermis, affecting improvement of SC barrier function and water-holding capacity (31). We can speculate that the combination treatment of IPL and TA injection softens scars and decreases scar size and height resulting in decreased total tensile strength and preserved cell-to-cell water-holding capacity. Consequently, the recovery of values of TEWL and SC capacitance was observed, preserving the softness and smoothness of the scar surface (14).

The side effects evaluated during the study were only mild and tolerable pain and transient erythema. None of the patients showed purpuric surface change after the combination treatment, whereas the most common side effect of 585-nm PDL treatment is postoperative purpura which can make many patients hesitate to initiate that kind of laser therapy (11,32). With IPL, the immediate and transient disappearance of the superficial visible vessels without residual epidermal whitening is the ideal end point of vascular lesions and correlates with the low incidence of post-treatment side effects (33). In the present study, all patients could do normal daily activity immediately after the treatment.
Although this study is limited by the absence of placebo control and direct comparison with PDL treatment group, to our knowledge, this is the first study to evaluate skin hydration status in keloids and hypertrophic scars treated by IPL with TA injection in Korean patients.

In conclusion, the combination treatment of IPL with TA injection can be a promising safe and effective non-surgical treatment option for patients with keloids and hypertrophic scars especially with restoration of skin hydration status to normal range. Further studies with a larger sample size and comparison of combined IPL and intralesional TA injection with PDL and intralesional TA injection or directly with intralesional TA injection monotherapy from the perspectives of skin hydration status are warranted.

Declaration of interest

None declared. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Supplementary material available online

Supplementary Figures 1–4.