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Evaluation of 5-aminolevulinic acid-mediated photorejuvenation of neck skin

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KEYWORDS
Photoaging;
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Red light;
Photodynamic therapy;
Thyroid

Summary
Objective: To evaluate the outcomes of the combination of red light or intense pulsed laser (IPL) with 5-aminolevulinic acid (ALA)-mediated photodynamic therapy (PDT) in the treatment of photodamaged neck skin.
Methods: The anterior of the neck was divided into four 2 cm × 2 cm sections and randomly assigned to red-light, red-light-PDT, IPL or IPL-PDT group. ALA cream of 5% was applied to PDT regions for 2 h prior to light irradiation. Treatment was repeated once. The stratum corneum (SC) hydration, transepidermal water loss (TEWL), L^*, a^*, b^* values, melanin index (MI), erythema index (EI), skin elasticity and skin thickness were examined by a blinded investigator. The function and volume of thyroid were also measured.
Results: After red-light-PDT, IPL-PDT and IPL treatment, the appearance of photoaging lesion was improved. The SC hydration, L^* value, elasticity and thickness increased, whereas the TEWL and MI value decreased. These changes in red-light-PDT and IPL-PDT group were more obvious than IPL group. The a^* and EI value increased in red-light-PDT group. No significant change was noticed in red-light group. Partial irradiation of the thyroid did not affect the function and volume of the thyroid.
Conclusion: IPL-PDT and red-light-PDT showed better rejuvenation effect than IPL or red light alone on the neck skin.

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Introduction

Skin aging is a progressive process in which environmental damages to the skin determine the appearance of aging. Among harmful environmental factors the long-term exposure to ultraviolet (UV) light is the most significant one and UV-induced skin aging is often referred to as photoaging [1]. The clinical signs associated with photoaging include laxity, wrinkles, dyspigmentation, a yellow hue, a leathery appearance, telangiectasia, and cutaneous malignancies in the sun-exposured area such as the face, neck and dorsum of hands [2]. Besides the long-term UV exposure, damages to the skin barrier can also promote skin aging [3].

Numerous studies suggest that topical photodynamic therapy (PDT) mediated by 5-aminolevulinic acid (ALA) is effective in repairing photoaging tissues [4—7]. Different light sources including red light, blue light, pulsed dye lasers (PDL), and intense pulsed light (IPL) have been used in PDT. Red light sources are used more often in China [8]. The combination of ALA and red light (red light-PDT) is proven effective in the treatment of photoaging skin [9]. IPL is a non-ablative treatment that uses high-intensity pulses of visible light to improve the appearance of vascular lesions, freckles, acne, and facial lines and wrinkles. IPL is one of the most popular non-ablative therapeutic modalities for photorejuvenation [10,11]. Several controlled trials have demonstrated that topical ALA could be used adjunctively to enhance the therapeutic effect of IPL on photoaging [12,13]. Recent anecdotal evidence also suggest that ALA PDT using IPL (IPL-PDT) as a light source might be superior to IPL alone for treating photorejuvenation [14].

Various non-invasive techniques have been developed to measure the biophysical properties of skin *in vivo* [11]. While an increasing body of evidence has shown the improvement of cutaneous photoaging after photorejuvenation treatment, few studies address changes in the biophysical properties of the skin, such as hydration, color, elasticity and thickness following photorejuvenation treatments. Understanding and adequate management of these changes after IPL treatments might prevent side effects and thereby enhance the clinical efficacy and safety of IPL-based therapies.

Although numerous therapeutic modalities for facial photorejuvenation are well documented, there is no report on the prospective study of PDT effect on photoaging skin of the neck. The differences between red light and IPL combination of ALA have not been reported yet. The aim of this prospective pilot study was to evaluate the efficacy and adverse effects of combining red light or IPL with topical ALA on the photorejuvenation of the neck skin.

Subjects and methods

Study design

This was a randomized, double-blinded and controlled prospective study. The neck area of subject should present at least a modest degree of photodamage. Inclusion criteria: the anterior portion of neck skin must have some of the following characteristic appearance of photodamaged skin according to the Glogau scale, such as sallow discoloration, inelasticity, rhytid formation, pigmentary alteration, ecstatic vessels, telangiectasias, and textural alterations [14,15]. Exclusion criteria: if affected areas received (1) ALA or red light, IPL, or other forms of radiation within 4 weeks, (2) topical retinoids or other skin care products containing hydroquinones, glycolic acids, or vitamin C within 4 weeks, (3) systemic retinoids within 6 months, (4) a likelihood of becoming pregnant and (5) active lactation. Participants were encouraged to use sunscreens (SPF of 30 or higher) daily during the trial period. Post treatment assessments were carried out by experienced dermatologists blindly. The study protocol and informed consent were approved by the research ethics committee of Shanghai Skin Diseases Hospital and all subjects were fully informed about the study and written consent was obtained from all participants.

Subjects

A total of 29 volunteers were screened and 24 met the inclusion criteria. All subjects were outdoor worker and had the Fitzpatrick skin types III or IV (50% *vs* 50%). First 14 were assigned to fluorescence examination group and following 10 to treatment group. The mean age of the fluorescence examination group was 45.9 ± 2.5 years old (7 females, 44—50 years old; 7 males, 42—48 years old). The mean age of treatment group was 41.4 ± 3.8 years old (5 females, 38—50 years old; 5 males, 39—46 years old).

In situ examination of PpIX production

Fourteen subjects were randomly and equally divided into two groups. Photoaging skin on the anterior of the neck was divided into four 2 cm × 2 cm sections using the center of the thyroid cartilage as the center point. In Group 1, 5% ALA cream (Fudan-Zhangjiang Bio-Pharmaceutical Co. Ltd., Shanghai, China) was evenly applied to four sections. The fluorescence intensity (FI) of PpIX was examined spectroscopically as described previously at 1, 2, 3 and 4 h, respectively [16]. In Group 2, 2.5%, 5%, 10% and 20% ALA cream was applied to four regions, respectively and incubated for 2 h before being subjected to the fluorescence examination. All measurements were in a darkened room and repeated five times.

Treatment protocols

Four neck regions of 10 subjects were randomly assigned to red-light, red-light-PDT, IPL or IPL-PDT group, respectively. The same amount of 5% ALA cream or basal cream (placebo) was uniformly applied to tested areas and covered by occluding dressing after the neck was washed with a mild cleanser. After 2 h of incubation, excess ALA cream and basal cream was removed and one ALA-applied area and one basal cream-applied area were covered with a layer of coupling gel and then irradiated with the Lumenis One IPL device (Lumenis, Inc., Santa Clara, CA USA) with a wavelength ranging from 520 to 1200 nm and spot size of 15 mm × 35 mm. Double or triple pulsing was used with the pulse width varying from 3.5 to 4.0 ms and a delay of 25 to 30 ms between