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ORIGINAL ARTICLE

"Multi Light and Drugs": a new technique to treat face photoaging

Comparative study with photorejuvenation

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Abstract Nonablative skin rejuvenation using laser, intense pulsed lights (IPLs), or radiofrequency techniques are becoming increasingly popular. In this paper, a novel protocol that integrates IPL sessions, low intense light and vitamin C, low-weight hyaluronic acid, betaglucan dermal injection versus IPL photorejuvenation as monotherapy is compared. A group of 100 patients, all women, with ages ranging from 35 to 65 years old (median age 56.3) with different degrees of photodamage was considered. A blinded control study was done. The patients were divided not randomly into two groups. These groups are similar for ages, skin types, and degrees of photoaging distribution. A first group of 40 patients had monotherapy consisting of seven sessions of IPL only. A second group of 60 patients had triple therapy consisting of seven sessions of IPL as well as nine sessions of low intense diode light and also biostimulation by drugs. Considering only the improvement in hyperpigmentations and teleangectasias, the monotherapy and the triple therapy show good results with no significant statistical difference between the two groups. Considering the improvement in skin texture and firmness in the group treated only with monotherapy, 30% (12 patients) had positive results, and 70% (28 patients) had poor results. In the group treated with triple therapy, 70% (42 patients) had positive results, and 30% (18 patients) had poor results, with the main differences in skin silicone negative imprints. On the basis of the data presented, the new technique of IPL, low intensity diode light, and multidrugs biostimulation seems to be a safe and effective method for skin rejuvenation and upgrades the effects of IPL in the fibroblasts' stimulation.

Keywords Intense pulsed light · Photorejuvenation · Biostimulation · Photoaging · Diode light

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Introduction

Skin changes in the elderly have been considered an inevitable and irreversible part of the aging process, with the undesirable texture and appearance masked with the use of cosmetics. Recently, however, there has emerged a clearer understanding that aging of the skin is the total of two processes: intrinsic changes associated with aging and extrinsic damage, particularly the accumulative effects of repeated exposure to actinic radiation, referred to as photoaging [1].

Photoaging is that damage done to the skin because of the direct effects of UV light. Clinically, the patient will present with skin that has a sallow complexion, with surface mottling, and a coarse thickened texture [2]. These structural changes will often be accompanied by other stigmata of sun damage including brown spotting (solar lentigines), telangiectasia, as well as actinic and seborrheic keratosis. Solar elastosis is the histological equivalent to clinical photoaging, and the terms are often used synonymously. Solar elastosis consists of deposition of massive amounts of abnormal elastic material, in the upper reticular dermis [3]. This increase in abnormal elastic fibers is accompanied by a corresponding decrease in amounts of collagen and a collagen-associated proteoglycan (decorin) [4].

Miyachi [5] noted that there was an evidence that cumulative UV light insults result in generation of reactive oxygen species (free radicals) and that the presence of these species are associated with cumulative structural changes associated with photoaging. Wlaschek et al. [6] noted that exposure to UV light type A (UVA 320–360 nm) led to an increase in reactive oxygen species, which in turn led to an up-regulation and synthesis of interstitial collagenase in vitro. Increased activity of interstitial collagenase would correlate with increased collagen degradation and connective tissue damage. Another type of damage caused by solar UV radiation on the skin is immunosuppression [7–9], which is characterized by depleted counts of Langerhans cell [10, 11] and inhibited contact hypersensitivity [12, 13].

Nonablative skin rejuvenation using laser, intense pulsed lights (IPLs) or radiofrequency techniques are becoming increasingly popular because of the aging population's desire for fresher, younger looking skin [14–19]. More and more patients are seeking noninvasive, no-downtime techniques to obtain smoother skin, diminish age spots and discoloration, and eliminate visible blood vessels.

This study aimed to analyze a new technique that integrates two system of light's skin exposure (IPL, low intensity diode light) with dermal injections of vitamin C, low weight hyaluronic acid, and betaglucan for the treatment and prevention of the face's photoaging versus IPL sessions as monotherapy.

Materials and methods

The data were collected over a 18-month period (January of 2005 to June of 2006). A group of 100 patients, all women, with ages ranging from 35 to 65 years old (median age 56.3) with different degrees of photodamage answered the questionnaire and permit to take digital photographs, and silicone negative impressions of their wrinkles before and 1 month after the last session were included in the study. The patients included had Fitzpatrick skin types II–IV: Twenty percent type II, 45% type III, and 35% type IV. All procedures were performed by one physician. Patients with any suspicion of skin cancer, skin pathology, or in doubt of pregnancy were not included. The patients signed a detailed informed consent.

The device used was Epi C® (Espansione Marketing s.p.a., Italy). The EPI-C unit is an IPLs and low intense diode lights source entirely controlled by a software that, among many functions, recognizes automatically the interchangeable lamps that are fitted onto the hand piece. The mixture of drugs for biorivitalization (vitamin C, low weight hyaluronic acid, and betaglucan) was HCG 2000® (Mavi Sud s.r.l., Italy). The hyaluronic acid molecular weight used for the mixture was 620–1,150 Da, and the density was 1 g/ml. The ascorbic acid molecular weight was 176.13 Da, and the density was 1.65 g/ml. The betaglucan was extracted from *Saccharomyces cerevisiae*, and its density was 1 g/ml.

A blinded control study was done. The patients were divided not randomly into two groups, trying to maintain these groups well matched for ages, skin types, and the degrees of photoaging. The skin type was classified using the Fitzpatrick skin types scale. The degree of photoaging was classified using the Glogau wrinkle scale, as follows: 1=no wrinkles, early photoaging: early pigmentary changes, no keratoses, and fine wrinkles; 2=wrinkles in motion, early to moderate photoaging: early senile lentigines, no visible keratoses, and smile wrinkles; 3=wrinkles at rest, advanced photoaging: dyschromia and telangiectasia, visible keratoses, and wrinkles at rest; and 4=only wrinkles, severe photoaging: yellowish skin color, previous skin malignancy, and generalized wrinkling.

A first group of 40 patients (median age 57.6 years), 20% Fitzpatrick skin type II, 45% skin type III, 35% skin type IV, 20% Glogau wrinkle scale 2, 75% wrinkle scale 3, and 5% wrinkle scale 4, had seven sessions of IPL as a single treatment. A second group of 60 patients (median age 55 years), 20% Fitzpatrick skin type II, 45% skin type III, 35% skin type IV, 25% Glogau wrinkle scale 2, 70% wrinkle scale 3, and 5% wrinkle scale 4, had seven sessions of IPL and also nine sessions of low intense diode light and drugs biostimulation. The "Multi Light and Drugs" technique starts with an IPL session and sessions of low intense diode light and drugs biostimulation after 1 week. After another week, an IPL session was done again and so on until the end of the scheduled therapies. The low intense diode light and drugs biostimulation session was done also every 30 days after the end, in summer, of the IPL protocol.

The IPLs sessions consist of multiple passages every time (three to four). The cutoff filter used was 550 nm. The fluence used varied between 20 and 30 J/cm^2 and the pulse duration varied from 10 to 20 ms, according to the skin type and the degree of photoaging. The interval between different sessions was 14 days.

The diode light skin exposure technology used is based on diode light at low intensity (623 nm and 40 mW/cm^2). The application time was 20 min and is divided into 50% at a fixed intensity emission and 50% at intermittent emission where 2 s are on a higher intensity emission phase and 1 s is on a lower emission phase. Five minutes after the diode light skin exposure, 5 ml of the mixture of vitamin C, low weight hyaluronic acid, and betaglucan (HCG 2000®) were injected superficially and deep in the dermis in multiple sites on the face spaced 1–2 cm (for an amount of 10–15 injections), especially in the cheeks. The needle used was 30 Gauge, and the infiltration was done in a net manner. The interval between different sessions was 14 days.

The mean duration of treatment was 20 min for IPL and 30 min for low intensity diode light and drugs biostimulation. At the end of the session, cold wet gauzes were applied to the skin for a few minutes. No creams or ointments were used after the procedure, and the patients were allowed to apply hypoallergenic makeup. A complete sun block was used before and after each treatment, and sun exposure was avoided as much as possible.

The patients filled out a detailed questionnaire concerning their satisfaction level, side effects, and complications 1 month after their last treatment. In the questionnaire, patient satisfaction was evaluated and graded on a scale from 0 to 5, with 5=excellent, 4=very good, 3=good, 2=moderate improvement, 1=mild improvement, and 0=no improvement. A nurse collected the patient rating at the office visit. A blinded dermatologist rated the results in hyperpigmentation, telangiectasias, skin texture, and firmness improvement by an accurate analysis of the patients before and after, of the images before and after, and of the negative silicone impressions of the chin, using the same scale of the questionnaire from 1 (no improvement) to 5 (excellent). The results obtained from the two groups were compared with the Chi-square test for statistical significance.

Results

The satisfaction rates for the patients are demonstrated in Table 1. In the group treated only with IPL sessions, two patients rate their global satisfaction 5, eight patients rate 4, four patients rate 3, 12 patients rate 2, eight patients rate 1, and six patients rate 0. Thirty-five percent (14 patients) have positive results (5-4-3 of the satisfaction scale), and 65% (26 patients) have poor results (2-1-0). In the group treated with the "Multi Light and Drugs" technique, nine patients rate their global satisfaction 5, 28 patients rate 4, five patients rate 3, eight patients rate 2, eight patients rate 1, and two patients rate 0. Seventy percent (42 patients) have positive results (5-4-3 of the satisfaction scale), and 30% (18 patients) have poor results (2-1-0 of the satisfaction scale). The Chi-square test demonstrates that the distribution is statistically significant (degrees of freedom=5, Chi-square=15.0799663299663, p is less than or equal to 0.025), so the "Multi Light and Drugs" technique makes the difference.

Table 1 Patient satisfaction rate

Patients global satisfaction							
	5	4	3	2	1	0	Total of patients
IPL	2	8	4	12	8	6	40
Light and Drugs	9	28	5	8	8	2	60
Total of patients	11	36	9	20	16	8	100

Table 2 Physician satisfaction rate for hyperpigmentations and teleangectasias

Physician satisfaction hyperpigmentations/teleangectasias							
	5	4	3	2	1	0	Total of patients
IPL	5	8	15	6	4	2	40
Light and Drugs	10	10	25	6	6	3	60
Total of patients	15	18	40	12	10	5	100

The Chi-square test results demonstrate no statistical significance between the two groups.

The satisfaction rates of the blinded dermatologist are reassumed in Tables 2 and 3. Considering only the improvement in hyperpigmentations and teleangectasias in the group treated only with IPL sessions, the rate is 5 for five patients, eight patients rate 4, 15 patients rate 3, six patients rate 2, four patients rate 1, and two patients rate 0. Seventy percent (28 patients) have positive results (5-4-3 of the satisfaction scale), and 30% (12 patients) have poor results (2-1-0 of the satisfaction scale). In the group treated with the "Multi Light and Drugs" technique, ten patients rate 5, ten patients rate 4, 25 patients rate 3, six patients rate 2, six patients rate 1, and three patients rate 0. Seventy-five percent (45 patients) have positive results (5-4-3 of the satisfaction scale), and 25% (15 patients) have poor results (2-1-0 of the satisfaction scale). The Chi-square test demonstrates that the distribution is not statistically significant (degrees of freedom=5, Chi-square=1.03009259259259; for significance at the 0.05 level, Chi-square should be greater than or equal to 11.07; p is less than or equal to 1), so the treatments show similar results.

Considering the improvement in skin texture and firmness in the group treated only with IPL sessions, the rate is 5 for two patients, four patients rate 4, six patients

Table 3 Physician satisfaction rate for skin texture/firmness

Physician satisfaction skin texture/firmness							
	5	4	3	2	1	0	Total of patients
IPL	2	4	6	5	13	10	40
Light and Drugs	10	22	10	8	5	5	60
Total of patients	12	26	16	13	18	15	100

The Chi-square test results demonstrate statistical significance between the two groups.

rate 3, five patients rate 2, 13 patients rate 1, and ten patients rate 0. Thirty percent (12 patients) have positive results (5-4-3 of the satisfaction scale), and 70% (28 patients) have poor results (2-1-0 of the satisfaction scale). In the group treated with the "Multi Light and Drugs" technique, the rate is 5 for ten patients, 22 patients rate 4, ten patients rate 3, eight patients rate 2, five patients rate 1, and five patients rate 0. Seventy percent (42 patients) have positive results (5-4-3 of the satisfaction scale), and 30% (18 patients) have poor results (2-1-0 of the satisfaction scale). The Chi-square test demonstrates that the distribution is statistically significant (degrees of freedom=5, Chi-square= 21.5722934472934, p is less than or equal to 0.001), so the new technique makes the difference (Figs. 1 and 2).

The most common side effect was persistent redness (12–18 h) for both groups of patients and ecchymosis in the group treated with the "Multi Light and Drugs" technique. No major complications or allergic reaction were seen.

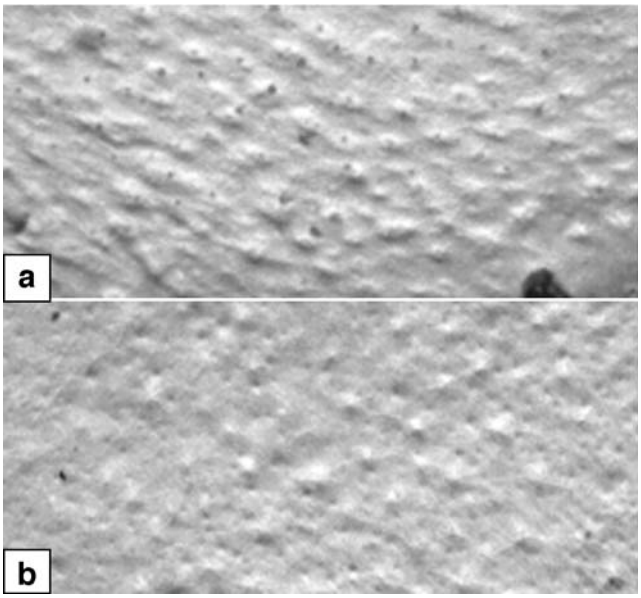

Fig. 2 Silicone negative imprints of skin texture before (**a**) and 8 months after "Multi Light and Drugs" (**b**). Skin texture improvement is evident

Discussion

Certainly, facial rejuvenation is an evolving art as well as a science. The main advantage of using nonablative IPL is that it allows a short recovery time with lower complication rates compared with the other methods such as laser resurfacing and chemical peeling. The IPL modality simultaneously affects lesions such as those that are vascular or pigmented. IPL is a noncoherent light produced by a flash lamp, which has been introduced over the past few years to improve the photodamage aspect of the skin. Using different cutoff filters allows selection of the desired wavelengths.

Recently developed photorejuvenation techniques address all the skin photoaging elements, which include rhytids, skin roughness, enlarged pores, telangectasia, redness, dyschromia, and solar lentiges. Contrary to laser skin resurfacing or chemical peels, photorejuvenation enables the elimination or significant reduction in these signs of photoaging on the face, neck, chest, or hands with little, if any, convalescence time and with minimal risk of adverse effects [20].

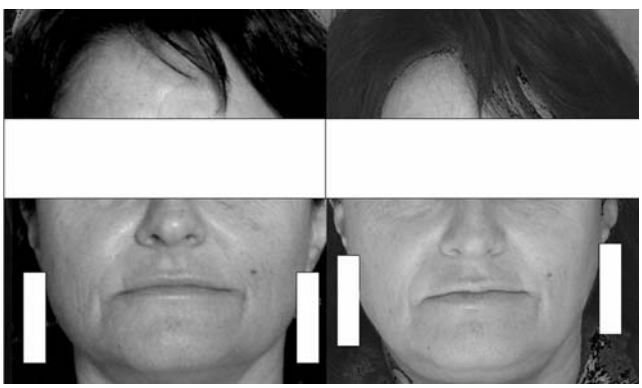

Fig. 1 49-year-old woman Pre and Post (6 months) after "Multi Light and Drugs." Skin texture and hyperpigmentations improvement are evident

The theoretical basis for photorejuvenation lies in the theory of selective photothermolysis [21] combined with the phenomena of neocollagenesis, which occurs in response to a mild thermal injury in the reticular and papillary dermis [22, 23]. The effect on the skin texture and general appearance is achieved by long waves that heat the collagen deep in the dermis, thus achieving some tightening of the skin. The effect on vascular and pigmented lesions is achieved by photothermal damage either to the blood vessels through absorption in hemoglobin or to the absorption in melanin-pigmented lesions. The light pulses and the delays between them, which are shorter than the thermal relaxation time of the epidermis, preserve it from the thermal damage. At the same time, the duration of the pulses and the delays are shorter than the thermal relaxation time of the targets, thus ensuring their selective destruction.

Among the nonablative modalities, neodymium:yttrium–aluminum–garnet was reported by Bitter [24] to be less beneficial to the epidermal lesions than the IPL. The redness after treatment usually lasts no more than a few hours, and the patients can go back to work shortly after the procedure using makeup. The procedure can be considered a "lunchtime" procedure. It is performed without any type of sedation, and it is easy to perform. The time needed to complete the facial area is only 20 min.

Unfortunately, photoaging is a complex process, so the treatments involved in its correction have to be done at

different levels. With the IPLs, most of the improvement was noticed for pigmented lesions and telangiectasias and much less for the skin texture, unlike Weiss et al. [25], which noticed skin textural improvement in 83% of the patients from their study. The skin is not a uniform layer, and telangiectasias, pigmented lesions, and collagen fibers are located within different levels and have different absorption coefficients. This is the reason for the need for more than one session, more than one wavelength, and the integration of drugs that correct reactive oxygen species (free radicals) as well as to stimulate neocollagenesis.

The new technique described above shows excellent results, both in the correction of facial teleangectasias and pigmented lesions as in skin texture changes compared with the use of IPL alone; that in the present study shows good results only in teleangectasias and pigmented lesions.

Light-emitting diodes (LEDs) are another form of light therapy that is a relatively recent development of the laser industry. LEDs are similar to lasers as much as they have the same effects but differ in the way the light energy is delivered. LED disperses over a greater surface area a low power energy that initiate the biostimulation process of cells. Low light energy is absorbed by the subcutaneous layers and stimulates cells activity and metabolism. The phenomenon of light absorption to produce electronic excitation of atoms and molecules has long been accepted by photochemists and photobiologists. When molecules are excited by light and immediately take part in chemical reactions, an improvement in the kinetics of the reactions is observed [26]. It was demonstrated that photodiode light irradiation at relatively low power levels influences fibroblast proliferation [27, 28], in in vitro culture with different mechanisms such as the activation of cells metabolism [29].

Moreover, various light wavelengths are reported to increase growth factor secretion from cultured macrophages [29]. The use of different wavelengths in low intensity diode light let us stimulate also endothelial proliferation and macrophage activation [29].

Biostimulation by dermal injection of different drugs is a well known procedure to re-establish the normal balance in collagen synthesis and reabsorption, to control melanogenesis, and to contrast the oxidative effects of UV exposure.

Ascorbate derivatives (vitamin C) suppress the effects of UV on human keratinocytes and fibroblasts [30], regulate epidermalization [31], make a free radical scavenging and stimulate extracellular matrix construction [32], stimulate collagen synthesis [33], and inhibit melanogenesis in vitro and in vivo [34, 35].

Low weight hyaluronic acid modulates proliferation and collagen and protein synthesis of fibroblasts [36], protects collagen against interleukin-1-induced inhibition of biosynthesis [37], and represents a multifunctional carbohydrate mediator of immune processes [38].

Betaglucan appears to stimulate the large white blood cells called macrophages into action. These cells are a primary defense system for our bodies, identifying abnormal conditions and activating the appropriate therapeutic response. They literally devour bacteria, foreign cells, dead and dying cells, mutated cells, cancerous cells, and other negative invaders. Betaglucan's stimulation of macrophage cells produces a cascade of immune events, boosting immune response, stimulating the production of immune cells, and improving host resistance. Besides the immunomodulatory effects, it has additional antioxidant properties [39] and stimulates human dermal fibroblast collagen biosynthesis through a nuclear factor-1-dependent mechanism [40].

The very good results obtained with the "Multi Light and Drugs" technique in the treatment of different degrees of photoaging let us assert that the technique can be also a prevention method for this alteration, especially in those cases when the signs of the photodamage are almost invisible. Moreover, the possibility of treating patients also in summer let us to go on with fibroblast stimulation and with the correction of reactive oxygen species (free radicals) in a period of the year of massive UV exposure. A long-term follow-up study will determine how long the good endpoints will last.

Conclusion

On the basis of the data presented in this article, we can conclude that the new technique described above of IPL, low intensity diode light, and multidrugs biostimulation seems to be a safe and effective method for skin rejuvenation. The short recovery time makes this procedure attractive for busy persons. The integration of three different procedures to correct photoaging signs is a new concept in aesthetic medicine. This is a method of global skin care, and this let us obtain better results in skin texture and firmness changes compared with the use of IPL alone as it is demonstrated in the results.

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