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NEW METHODS AND TECHNIQUES

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SUPPLEMENT

ACNE • ROSACEA • VITILIGO • MELANOMA • PSORIASIS
COSMETICS • IMPLANTS • NAILS • IMMUNOMODULATORS

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A LETTER FROM THE EDITOR-IN-CHIEF

5-Aminolevulinic Acid Photodynamic Therapy: A Therapeutic Platform in Dermatology

Over the last few years, many journal articles have been published highlighting the promise and potential broad clinical utility of topical 5-Aminolevulinic Acid (5-ALA) Photodynamic Therapy (PDT) in dermatology. Levulan® (20% 5-ALA from DUSA Pharmaceuticals, Inc.) was FDA approved with blue light (BLU-U® from DUSA Pharmaceuticals, Inc.) in 2000 for the treatment of multiple actinic keratosis (AK) of the face or scalp.

Initially, in the United States ALA was not well-received or widely adopted, since the procedure was logistically cumbersome, many patients complained of pain during light treatment, and the reimbursement for treating AKs was unacceptable. Since 2000, researchers and early adopters of the new therapy have found ways to not only make the procedure much more practical and far less cumbersome, but side effects have been reduced to a mild to moderate sunburn for only a few days post treatment. Short contact, broad area application of ALA using a variety of light sources that already exist in our practices today has clearly widely opened the possibility for using this topical therapy for many applications in dermatology.

In this supplement, Dr. Gold and Dr. Taub have highlighted results from their studies using ALA for the treatment of acne vulgaris and sebaceous gland hyperplasia. Both are conditions that dermatologists deal with every day and for which there is a clear need for new therapeutic advancements and treatments. Also, within this supplement I have selected two out of the five winning case reports from the recent PDT Case Report Contest.

ALA has a very bright future and given that every month we continue to read and hear about new and exciting applications for this therapy, in my opinion it should be viewed as a therapeutic platform in dermatology. I hope that you will find this supplement useful and educational and continue to offer us feedback through your letters to the editor, case reports, and article submissions.

Perry Robins, MD

Editor-in-Chief, Journal of Drugs in Dermatology
Professor of Dermatology, NYU Medical Center

Treatment of Sebaceous Gland Hyperplasia by Photodynamic Therapy with 5-Aminolevulinic Acid and a Blue Light Source or Intense Pulsed Light Source

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Abstract

Treatment of SGH by ALA-PDT with Blue Light Source or Intense Pulsed Light Activation. Sebaceous gland hyperplasia (SGH) lesions often present as a sign of photoaging and have proven difficult to treat. Photodynamic therapy (PDT) may be an effective treatment option. Twelve patients with SGH received PDT with 5-aminolevulinic acid (ALA, Levulan® Kerastick®, DUSA Pharmaceuticals, Inc) photosensitizing agent topically applied with a 30- to 60-minute drug incubation period. Patients received either 405-420 nm blue light (ClearLight™ PhotoClearing System, CureLight, Lumenis) for 15 minutes or intense pulsed light (IPL), 500-1,200 nm and 550 nm cut-off filter (VascuLight™ System, Lumenis) according to a randomization protocol. ALA-PDT was administered once per month for 4 consecutive months. Progress was evaluated at 4 and 12 weeks after the final treatment. More than a 50% reduction in the number of SGH lesions was achieved for patients in both treatment arms without lesional recurrence during the treatment and follow-up periods. All treatments were well-tolerated. Adverse effects were limited to mild, transient erythema (n=2) and blisters (n=1), which resolved without sequelae. ALA-PDT with either blue light or IPL photoactivation may provide therapeutic benefit without significant adverse effects in patients with SGH.

Introduction

Sebaceous gland hyperplasia (SGH) is often seen in both medical and cosmetic dermatology practices. In certain patients, SGH lesions are a benign manifestation of photoaging. Lesions range in size from 2 mm to 4 mm and occur as flesh-colored, papular aggregates that arise from proliferating sebaceous glands. A ductal opening or central umbilication is usually present in the lesions.

For SGH, reports of treatment modalities that do not result in scarring or other textural changes in skin are lacking. Topical medications yield inconsistent results and surgical options are limited by pain, prolonged healing times, scarring, and lesional recurrences. Treatment with the pulsed dye laser (PDL) alone, however, has shown promising results in patients with SGH[1].

The dermatologic use of photodynamic therapy with topical 5-aminolevulinic acid (ALA-PDT) and a variety of lasers and light sources has been reviewed[2,3]. A potent skin photosensitizer, ALA acts as a prodrug that penetrates the stratum corneum and accumulates selectively in both dystrophic/actinically damaged skin cells and sebaceous glands. Within these cells, ALA is transformed into photoactive protoporphyrin IX (PpIX). Exposure of PpIX to wavelengths of light within PpIX's absorption curve[4] produces singlet oxygen that destroys cells containing PpIX.

ALA-PDT is commonly used to treat nonhyperkeratotic actinic keratoses of the face and scalp as well as superficial basal cell and squamous cell carcinomas. Recent reports also indicate efficacy in moderate to severe acne and in all parameters of photorejuvenation. Blue light, vascular lasers, and the intense pulsed light (IPL) have been successfully used to activate PpIX[3].

Because topical ALA accumulates in pilosebaceous units of the skin and is metabolized to photosensitive PpIX5-8, it appeared logical to further study the efficacy of ALA-PDT in the treat-

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ment of SGH. ALA-PDT with photoactivation by (1) polychromatic light from a slide projector[9], (2) PDL[10], and (3) blue light[11] have been used successfully to treat SGH lesions.

Materials and Methods

The clinical trial was performed at the Tennessee Clinical Research Center in Nashville, Tennessee under the auspices of the Western Institutional Review Board (WIRB) in Seattle, Washington. All patients gave signed informed consent before participating. Patients receiving topical or systemic medications for SGH or with a history of light-based treatment were excluded. A minimum of 5 SGH lesions were required to participate. All SGH lesions were located on facial skin and identified visually by a board-certified dermatologist.

Twelve patients enrolled in the trial and received ALA-PDT with topical ALA (Levulan® Kerastick®, DUSA Pharmaceuticals, Inc.) photosensitizing agent. ALA was applied to the entire face without occlusion. After a 30- to 60-minute drug incubation, ALA was removed with Cetaphil® Cleanser (Galderma). Patients were treated randomly (alternating treatment modalities) with either the ClearLight™ PhotoClearing System, (CureLight™, Lumenis, Inc.) or a 500- to 1200-nm IPL source (VascuLight™ System, Lumenis, Inc) with a 550-nm cut-off filter. The ClearLight™ PhotoClearing System emits high-intensity 405- to 420-nm blue light. Patients received 15 minutes of blue light therapy without anesthesia or cooling. IPL treatment parameters included 32 J/cm2 fluence, 3.5/3.5-msec pulse duration, and 20-msec pulse delay time. ALA-PDT treatment was given once per month for 4 consecutive months. Progress was evaluated visually with lesion counts at each visit and photographic analysis at each visit and at the 4- and 12-week follow-up sessions.

During the treatment and follow-up periods, patients received no other forms of therapy for SGH and no cleanser other than Cetaphil was used.

Results

Eleven patients (91.7%) aged 42 to 61 years (median 52.3 years) completed the study. The remaining patient was disqualified for using prohibited skin care products during the follow-up period.

The 6 patients with blue light activation showed an average 50.6% reduction in SGH lesion count at the end of the 4-month treatment period. The average reduction increased to 55.3% 4 weeks after the final treatment and remained at 55.3% at 12 weeks. No lesions returned during the treatment and follow-up periods.

The 5 patients with IPL activation showed an average 48.4% reduction in SGH lesion count at the end of the 4-month treatment period. Average reductions increased to 53.4% 4 weeks after the final treatment and remained at 55.3% at 12 weeks. No lesions returned during the treatment and follow-up periods.

Adverse effects were limited to minimal erythema persisting for 48 hours after ALA-PDT in 2 patients and a small blister that resolved within several days without sequelae in one other patient. A clinical example of a patient treated with ALA-PDT and IPL is shown in Figures 1A and 1B.

Discussion

A variety of treatment modalities have been used for SGH lesions. Topical medicines have not proven worthwhile; surgical approaches, including cryotherapy, excision, electrodesiccation, CO_2 laser therapy, and oral therapy with isotretinoin have been associated with SGH lesional recurrence and unacceptable adverse effects[10].

Using a 20% solution of ALA and a slide projector light source, Horio et al[9] reported the first successful treatment of SGH with PDT. The authors treated facial lesions of a 61-year-old Japanese man three times at 1-week intervals. The photosensitizing agent was in contact with the treated areas for 4 hours. Although the lesions did not fully resolve, they became smaller with each successive treatment and their reduced sizes persisted for 1 year. The treatments were well-tolerated.

Other authors have reported encouraging results with shorter ALA incubation times in treating SGH lesions. Alster and Tanzi[10] treated SGH lesions in 10 patients with ALA (Levulan Kerastick) and 595-nm PDL activation of the drug. The incubation time for the ALA was for 1 hour and patients received either one PDL treatment or two treatments at a 6-week interval. For comparison, the authors used matched lesions on the same patients—some left untreated and others treated with PDL alone. Patients were evaluated regularly for 3 months. When topical ALA and PDL irradiation were used in combination, lesions were cleared with a single treatment in 7 patients and with 2 treatments in 3 patients. Improvement with the combination was noted to be superior to that of PDL alone. The untreated lesions did not change during the treatment period. All treatments were well-tolerated by the study participants.

Richey and Hopson[11] also treated 10 patients with SGH lesions using ALA-PDT and a short 1-hour ALA drug incubation time. These authors irradiated the SGH lesions with 410-nm blue light (BLU-U®, DUSA Pharmaceuticals, Inc.). Patients were given 3 to 6 treatments spaced 1 week apart and were followed for 6 months. All patients responded at least partially

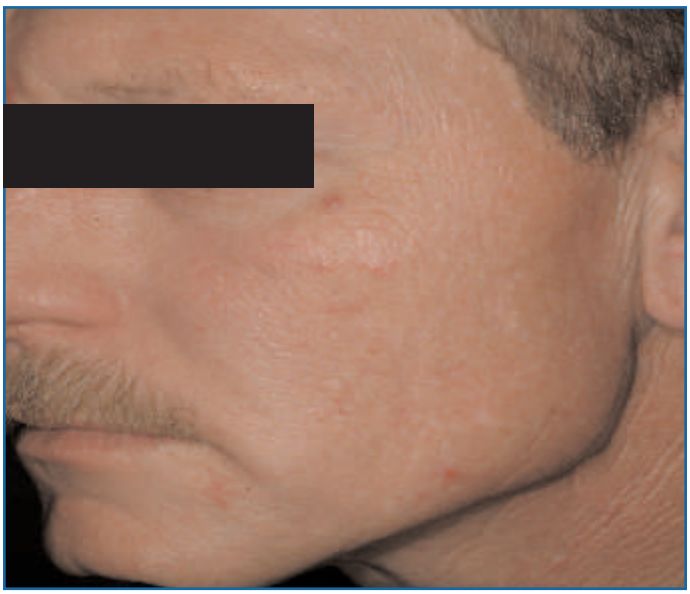

Figure 1A. Sebaceous gland hyperplasia lesions on the patient's cheek before photodynamic therapy with topical 5-aminolevulinic acid photosensitizing agent and intense pulsed light activation.

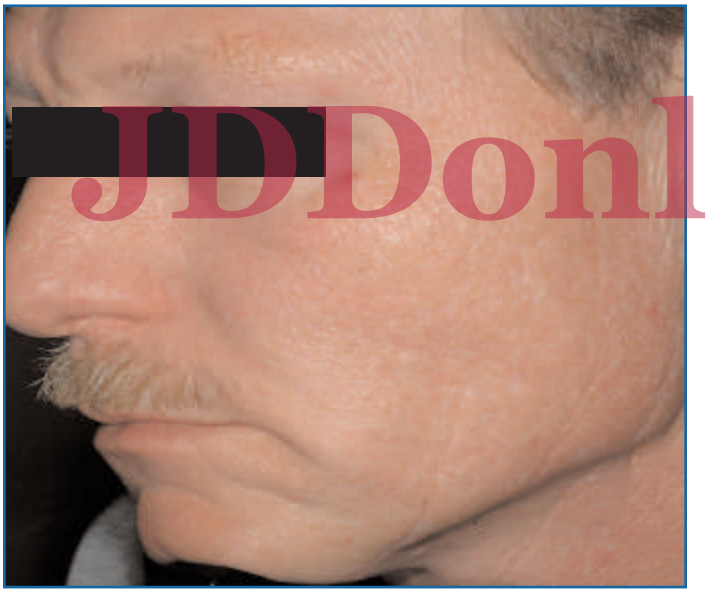

Figure 1B. Reduction in sebaceous gland hyperplasia lesion counts on the patient's cheek 3 months after four treatments.

with no scarring noted by the authors. By the last treatment, 70% of treated lesions (on average) were cleared and did not recur during the 6-month follow-up period. Recurrence rates up to 20% were seen within 3 to 4 months after the final treatment.

Goldman[12] reported his results with ALA-PDT and full-face, short-contact ALA drug incubation with either IPL or high-intensity blue light activation for both acne vulgaris and SGH lesions. Lesions were noted to be relatively clear after 2 to 4 treatments. Treatments were pain free and without adverse effects.

Touma et al[13] showed that 1-hour ALA drug incubation was as effective as 3-hour and even 14- to 18-hour drug incubation in ALA-PDT for actinic keratoses and photodamaged skin. For our SGH study, we chose to use 30-minute to 1-hour ALA incubation, although our experience, combined with other clinical investigations, suggests that a 1-hour incubation yields better results than shorter drug incubation times because the longer drug incubation time maximizes the absorption of the ALA into the sebaceous glands.

The results of our study suggest that ALA-PDT with either the blue light or the IPL for drug activation is a promising option for difficult-to-treat lesions of SGH. Additional studies to optimize ALA-PDT treatment strategies are warranted. For example, preoperative microdermabrasion or acetone scrubbing (not performed during our clinical trial) prior to the application of ALA may enhance ALA penetration and give better results. More frequent treatments at shorter intervals, i.e., one time per week or every other week, may also improve results. This, too, needs further study.

We can conclude, however, that ALA-PDT should be considered a first-line therapy for lesions of SGH. It is safe, effective, and has been demonstrated useful with a variety of lasers and light sources.

Dr. Gold is a consultant for DUSA Pharmaceuticals, Inc, and Lumenis, Inc. Dr. Gold performs research for, speaks for, and owns stock in both companies. Levulan® was provided by DUSA Pharmaceuticals, Inc. The ClearLightTM PhotoClearing System and VascuLightTM System were purchased at a discounted price from Lumenis, Inc.

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Photodynamic Therapy for the Treatment of Acne: A Pilot Study

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Abstract

Photodynamic therapy (PDT) with use of topical 5-aminolevulinic acid (ALA, Levulan® Kerastick®, Dusa Pharmaceuticals, Inc., Wilmington, MA) photosensitizing agent is a new modality for the treatment of acne. Eighteen patients (aged 15 to 63) with moderate to severe inflammatory acne received ALA-PDT. ALA remained in contact with skin for 15 to 30 minutes before exposure to blue light (ClearLight™ [Lumenis] or BLU-U® [Dusa Pharmaceuticals, Inc.]) or the Aurora DSR™ (Syneron Medical Ltd.), which uses Electro-Optical Synergy (ELOS™), a unique combination of optical and radiofrequency (RF) energy. Patients received two to four ALA-PDT treatments over four to eight weeks or two cycles of ALA-PDT (weeks 2, 4) preceded by salicylic acid peel (weeks 1,3) over four weeks. The average follow-up time was four months. On a scale of 0.0 to 4.0, the average acne grade improvement was 1.75. Among the 12 patients who said their acne had improved, 11 had at least 50% improvement and five had more than 75% improvement. Adverse effects were limited to erythema and peeling for up to five days after treatment and one episode of impetiginization of the affected area. Patients with moderate to severe acne can achieve durable improvement with short-contact ALA-PDT.

Introduction

Photodynamic therapy (PDT) is a new treatment for acne that involves the topical application of 20% 5-aminolevulinic acid (ALA [Levulan® Kerastick®]) to the affected area and irradiation with light or laser. ALA is absorbed preferentially by the sebaceous gland, where it is metabolized to protoporphyrins (primarily protoporphyrin IX [PpIX]), that absorb significant amounts of blue, red, and yellow light. Subsequent irradiation leads to photodestruction of *Proprionibacterium Acnes (P. Acnes)* as well as shrinkage or destruction of sebaceous glands, potentially leading to long-term therapeutic efficacy[1,2].

With maximum absorption at 410 nm (blue) and smaller peaks at 505, 540, 580, and 630 nm, PpIX has been activated by a variety of lasers and light sources[3] in the PDT treatment of acne.

The use of blue light activation in PDT is well established[4]. The Aurora DSR™ (Syneron Medical Ltd.) uses Electro-Optical Synergy (ELOS™), a unique combination of optical (580-1000 nm) and RF energy[5,6]. The purpose of this study was to obtain preliminary data on the efficacy and safety of using blue light, ELOS, and combinations of these light sources to activate photosensitizer in the PDT for acne.

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Materials and Methods

Eighteen patients (13 women, 5 men) with moderate to severe inflammatory acne were given ALA-PDT without anesthesia or cooling. Patients (Fitzpatrick skin types 1-3) were aged 15 to 63 years (mean 35), had failed conventional therapy for acne, were willing to undergo PDT, and had no additional cutaneous or non-cutaneous co-morbidities. The average duration of acne was 12 years. Eight patients had taken isotretinoin and 15 had taken oral antibiotics. Patients were excluded if they were pregnant, receiving isotretinoin, or unwilling to avoid sunlight for 48 hours after PDT. All patients gave informed consent to treatment.

ALA was not only applied to individual acne lesions but to the entire affected area. The skin was prepared by performing an acetone scrub and an alcohol scrub. ALA remained in contact with skin for 15 to 30 minutes before irradiation. ALA was removed with acetone and alcohol. Photosensitizer was activated by one or both of the following: 417- to 420-nm blue light (ClearLight™ [Lumenis] or BLU-U® [Dusa Pharmaceuticals, Inc.]) or the Aurora SR™.

Table 1. Results of Photodynamic Therapy for Acne

Patient no./Sex/Age/treated area	Acne Duration (yrs.)	Previous Tx				Tx Details: Incubation time–min (Light exposure – mins or ELOS settings)			Total Tx (PDT)	Improvement* (Follow-up, mo)
		Isotretinoin	Antibiotics	Oral Contraceptive	Other	BLU-U	ClearLight	Aurora		
1/F/45/face	20					—	15 (3)	—	2	2.5 (8)
2/F/40/face	24	X	X	X	Dermabrasion	15 (7)	—	15(29J, 25 RF)	2	0 (2)[1]
3/F/22/face	9	X	X	X	—	—	—	30 (25-30J, 25 RF)	4	2 (0)[2]
4/F/48/face	10	—	X	X	—	—	15 (3)	15(16-20J, 16-20RF)	8	3 (3)[3]
5/F/46/back	20	X (x 2)	X	—	—	—	30 (5)	—	2	0 (1)[4]
6/M/23/chest, back	1	—	X	—	—	—	30 (12-15)	—	2	2.5 (4)[5]
7/F/56/face, chest, back	25	X (x 4)	X	—	—	30 (6-8)	30 (6-12)	—	5	2.5 (2)
8/M/58/face	20	X (x 3)	X	—	—	—	—	30 (15-22J, 15RF)	3	3 (12)[6]
9/M/22/face	6	—	X	—	—	30 (4)	—	—	2, peel	0 (2)
10/M/28/face, back	12	—	X	—	—	—	15-30 (4-7)	—	3	3 (4)[7]
11/F/19/face	1	—	—	—	—	—	15 (3)	—	3	0 (1)[8]
12/M/63/face	35	X	X	—	—	—	30 (4-9)	30 (12-18J, 18 RF)	3	2.5 (3)
13/F/39/face	7	—	X	—	—	—	30 (4)	—	2	3.5 (1)[9]
14/F/17/face	4	—	X	—	—	—	15 (4)	—	3	1 (2)
15/F/26/face	13	—	X	—	—	15 (5)	—	—	3	3.5 (6)
16/F/15/face, cheek	2	—	—	—	—	15 (3)	—	—	2, peels	0 (4)[10]
17/F/45/face	10	X	X	—	—	15-30, (4)	—	—	2	0 (4)[11]
18/F/19/face	5	—	X	—	—	—	—	30 (25J, 25 RF)	1	2.5 (16)[12]

* Improvement graded on a scale of 0.0 to 4.0 (0 = no improvement, 4.0 = maximum improvement).
1 Six month decreased redness of rosacea with 1st Tx; flared after 2nd Tx.
2 Improvement lasted one month, then flared.
3 First course of ELOS resulted in 75% improvement in texture, sebaceous gland hyperplasia, and redness; acne improved with second course of blue light.
4 Flare, impetiginized.
5 No adverse effects.
6 Significant decrease in rosacea flares; mild peeling, redness for 5 days. Coming in for maintenance once every 6 months – did better with ELOS than blue light.
7 Peeling, redness; patient's skin became much smoother ("pebbling" was gone) and patient plans to have maintenance treatment every 2 months.
8 Moderate peeling, redness for 1 week after first Tx.
9 Acne recurred 2 months after Tx.
10 Patient switched to isotretinoin.
11 Patient switched to isotretinoin.
12 Significant decrease in acne scarring; peeling and erythema for 4 days, followed by marked decrease in erythema overall.

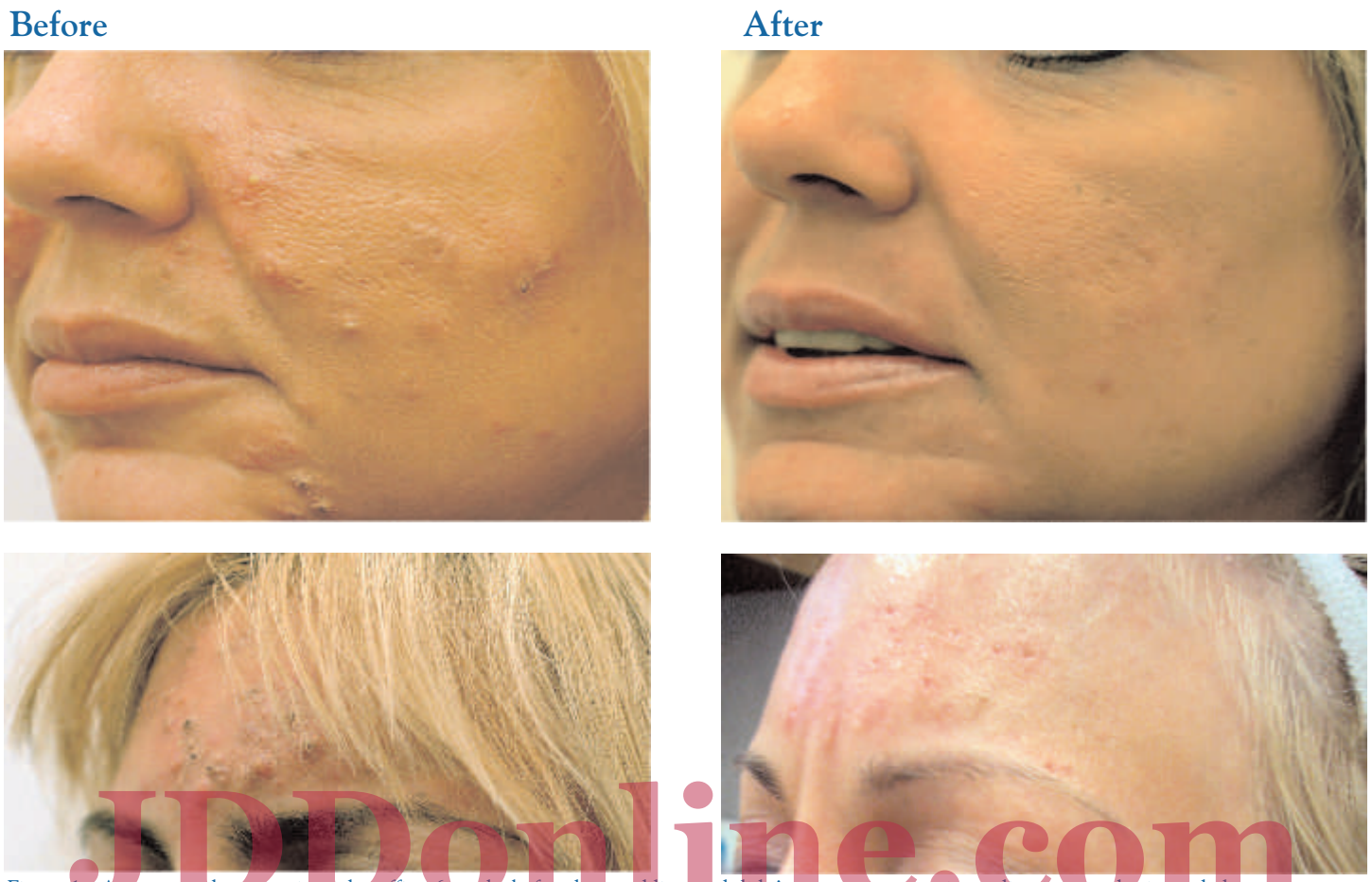

Figure 1. A woman who came into the office 6 weeks before her wedding and didn't want any systemic medications as she intended to get pregnant on her honeymoon. She is currently 7 months pregnant. (Patient #13, Table 1.)

Patients were exposed to blue light (BLU-U or ClearLight) for 3 to 7 minutes, one short pass of pulsed light ELOS (18-25 joules/cm^2 and 18-20 joules/cm^3 of RF energy).

Improvement was graded on a scale of 0.0 to 4.0 (0 = no improvement, 4.0 = 100% improvement).

Patients received two to four ALA-PDT treatments over four to eight weeks or two cycles of ALA-PDT (week 2,4) preceded by salicylic acid peel (weeks 1,3) over four weeks. A total of 51 treatments were given. Patients were followed for up to 1 year after the final treatment. Results were evaluated visually by examining photographs taken before and after treatment. Progress was evaluated at 1, 3, 6, and 12 months after the final treatment. Not all patients were available for each scheduled follow-up visit.

Results

Twelve of the 18 patients said their acne had improved with the treatment (Table 1). The average acne grade improvement was 1.75. Eleven of these patients had at least 50% improvement and 5 had more than 75% improvement. Five patients did not improve and flares occurred in two of these five.

Acne lesions have not recurred in one patient and 2 patients have had more than 12 months free of acne. Two more have achieved remission for more than six months. The average follow-up was four months. Two of the 11 patients who did well initially experienced a recurrence at one and two months respectively.

Adverse effects were limited to erythema and peeling for up to five days after treatment and one episode of impetiginization of the affected area.

Discussion

The results show that short-contact ALA-PDT can result in durable improvement in patients with moderate to severe acne who had failed traditional systemic medications.

Other investigators have reported success in the treatment of acne with ALA-PDT with various light sources. Hypothesizing

that ALA-PDT would attack *P. acnes*, sebaceous glands, or both, Hongcharu et al[7] conducted a study involving 22 patients with mild to moderate acne on their backs. Each patient was given four separate treatments, each at a different site: (1) ALA (Levulan® Kerastick®), (2) red light, (3) ALA and red light, and (4) no treatment. ALA was in contact with lesions for three hours before treated areas were irradiated. Half the patients were treated once and the other half were treated once a week for four consecutive weeks.

Only patients receiving ALA-PDT with red light responded to treatment. A single ALA-PDT session resulted in significant clearance for up to 10 weeks and four treatments resulted in clearance for up to 20 weeks. Adverse effects included erythema, exfoliation, and hyperpigmentation after treatment.

After having success with pulsed excimer-dye laser (635 nm) activation in the ALA-PDT treatment of a single patient with intractable facial acne[8], Itoh et al[9] substituted less expensive polychromatic visible light (600-700 nm) for the laser in the ALA-PDT treatment of 13 additional patients with intractable acne. As in the earlier study, ALA was in contact with treated areas for four hours before irradiation. After a single treatment, facial appearance improved in all patients and new acne lesions were reduced at 1, 3, and 6 months. Adverse effects included burning/stinging during irradiation and post-treatment edematous erythema, epidermal exfoliation, and pigmentation.

Goldman and Boyce[10] used blue light with and without ALA to treat 22 patients with mild to moderate acne. Patients given ALA-PDT with blue light activation were treated twice with two weeks between treatments, whereas patients given only blue light were treated once a week for two weeks. Both groups were evaluated two weeks after the final treatment. For acne severity, the authors reported 32% improvement in patients treated with ALA-PDT and blue light compared to 25% in patients treated with blue light alone. Respective reductions in papule counts were 68% vs. 40% whereas pustule count reductions were 61% vs. 65%. Neither treatment group experienced serious adverse events or significant pain.

Blue light was utilized in the present study because (1) this wavelength (417 nm) corresponds with the maximum absorption peak of PpIX, (2) the blue light source is easy to use, and (3) patient discomfort with the procedure is minimized. The ELOS technology was used because, in the author's experience, treatment with the Aurora's combination of optical and RF energy provides more improvement in skin texture than optical energy (as intense pulsed light [IPL]) alone. The broadband pulsed light of the Aurora should activate the ALA in the 580-630 nm range. IPL has been shown to be effective for PDT for rejuvenation[11].

This author hypothesized that the ELOS device, when used in PDT, might provide greater efficacy than blue light because (1) the longer wavelengths (580-1000 nm) of light penetrate more deeply into skin than the 417-nm blue light, (2) specific absorption occurs in the vascular spectrum, and (3) the textural improvement might be greater with the addition of ELOS. Although too few treatments were performed to determine the efficacy of ELOS in PDT, improvements in five of six patients treated with ELOS were significant, with grades ranging from 2.0 to 3.0. Thus, ELOS as an activator in PDT appears to be effective in this limited sample.

An important aspect of treating acne with PDT is minimizing adverse events. Most adverse effects have been theorized to be due to continued activation of PpIX (by sunlight and even bright indoor light) despite thorough removal of ALA solution from the skin. Since PpIX has a half-life in the skin of approximately 30 hours[12], a reservoir of ALA, inactivated PpIX, or both might remain on, or in, the skin. Shortening irradiation time or ALA incubation time could potentially reduce adverse effects, but may also reduce efficacy.

Another hypothesis currently being tested is the use of topical ferric chloride, which might theoretically "quench" the remaining porphyrin by converting it to the non-light-absorbing heme molecule.

Conclusion

This study confirms that patients with moderate to severe acne can achieve durable improvement from PDT. Very short contact was utilized, making this treatment protocol easier to administer than those based on more prolonged incubation times. Both blue light and an intense pulsed light with radiofrequency device (ELOS) were effective. Most of our patients had intractable, chronic acne and had failed potent systemic medications, making this success more notable.

With continuing concern over the safety issues of long-term systemic antibiotics and isotretinoin, this new therapy represents a major advance in our therapeutic armamentarium for acne. Further studies to determine ideal treatment algorithms, differential results with various light sources, incubation times, techniques for reducing adverse events and repeatable results are in process and needed to advance this new modality.

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The Use of a Novel Intense Pulsed Light and Heat Source and ALA-PDT in the Treatment of Moderate to Severe Inflammatory Acne Vulgaris

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Abstract

The use of lasers and noncoherent light sources is becoming more commonplace in the treatment of inflammatory acne vulgaris. Topical 5-aminolevulinic acid (ALA) is finding its niche as an enhancer to these laser and light sources. Twenty patients with moderate to severe inflammatory acne vulgaris were enrolled in a clinical trial to evaluate the efficacy of ALA-PDT with activation by a SkinStation® LHE® (Radiancy, Inc., Orangeburg, NY), a novel intense pulsed light (IPL) and heat source that emits 430-nm to 1100-nm radiation at 3 to 9 J/cm2 fluences. Patients were given topical ALA (Levulan® Kerastick®, Dusa Pharmaceuticals, Inc., Wilmington, MA) photosensitizing agent that remained in contact with skin for one hour before irradiation. Fifteen patients completed the trial and 12 responded to the treatment. Among respondents, reduction in active inflammatory acne lesions was, on average, 50.1% at the end of the 4-week treatment period, 68.5% 4 weeks after the final treatment, and 71.8% 12 weeks after the final treatment. ALA-PDT with IPL activation was well-tolerated by all patients. No treated lesion recurred at the end of the follow-up period. ALA-PDT with IPL activation is a treatment option for patients with moderate to severe inflammatory acne vulgaris.

Introduction

A difficult disease to treat, acne vulgaris (acne) accounts for more than 30% of all visits to dermatologists. Approximately 80% of the population will suffer from this condition at some time[1]. Acne affects more than 40 million American adolescents and approximately 25 million American adults[2].

Acne is a multifactorial disease. Both genetics and hormonal changes that begin during puberty play a role in its development. In its simplest form, acne is a disorder of the sebaceous glands where hormonal activity results in glandular dilation, obstruction, and proliferation of *Propionobacterium Acnes (P. Acnes)* bacteria. This is clinically evident as the papules, pustules, and cystic lesions characteristic of inflammatory acne vulgaris.

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Treatment options for acne include topical and systemic antibiotics, topical benzoyl peroxides, topical salicylic acid, and topical and systemic retinoids. Use of these agents, however, is often difficult and frustrating. Topical medications may irritate the skin and require several months for a positive response. Antibiotic resistance rates up to 60% have been reported [1,3] and long-term use of tetracycline may increase the risk of breast cancer[4]. Finally, lay press reports of teratogenic and psychological problems associated with systemic retinoid therapy have raised concerns about these drugs.

Exposure to ultraviolet (UV) light has been reported effective against acne vulgaris by researchers[5] and patients. Although not fully understood, the mechanism of the UV effect presumably involves destruction of *P. Acnes* in the sebaceous gland, leading to lesional resolution. The potential of UV exposure to cause photoaging and skin cancer preclude its regular use in the treatment of acne.

Photodynamic therapy (PDT) requires a photosensitive compound, light, and molecular oxygen to kill cells[6,7]. As *P. Acnes* proliferates in sebaceous glands, they produce protoporphyrin IX (PpIX) and coproporphyrin III, both of which demonstrate an absorption maximum at 415 nm, in the range of blue light with a second peak in the red light range (630 nm) and several smaller peaks in between blue and red light[8]. When these

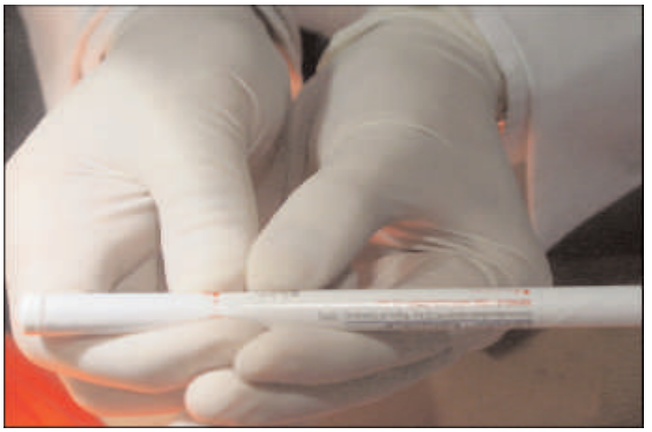

Figure 1. Levulan® Kerastick® manufactured by DUSA Pharmaceuticals, Inc.

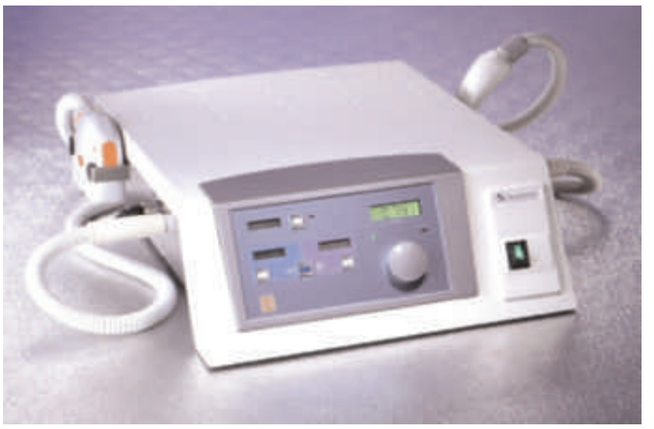

Figure 2. SkinStation® manufactured by Radiancy, Inc.

photosensitive porphyrins are irradiated with blue light, the singlet oxygen produced selectively destroys the bacterial cells and clears the acne lesions. Clinical trials[9-14] have shown the effectiveness of endogenous PDT with blue light in mild to moderate inflammatory acne. Several laser and light-based systems, including an intense pulsed light (IPL) and heat source (LHE®), have also been shown to be effective in the treatment of mild to moderate inflammatory acne[15-18].

To enhance the photodynamic reaction and potentially treat moderate to severe inflammatory acne, investigators began to use an exogenous form of PDT in which a photosensitizing agent, 5-aminolevulinic acid (ALA), is topically applied to the area to be treated before light treatment[19]. As part of the natural biosynthetic pathway for heme, topical ALA enters the skin and is converted to the photosensitive PpIX. Activation of PpIX, again by light of an appropriate wavelength, leads to the formation of cytotoxic singlet oxygen[6,7]. The use of the exogenous ALA is thought to act in a synergistic manner to enhance the photodynamic reaction.

The applications of ALA-PDT in dermatology—including actinic keratoses, superficial basal cell carcinoma, squamous cell carcinoma, Bowen's disease, and other cutaneous conditions—have been thoroughly reviewed[6,7,20-23]. More recent uses are in the treatment of recalcitrant verrucae vulgaris and molluscum contagiousum[24] as well as hidradenitis supporitiva[25].

Since reports suggest that acne vulgaris[26-31] and sebaceous gland hyperplasia[29,32,33] respond to ALA-PDT, we evaluated the efficacy of short-contact, full-face ALA-PDT with a novel light and heat (LHE) technology for the treatment of moderate to severe inflammatory acne vulgaris.

Materials and Methods

The clinical trial was performed at the Tennessee Clinical Research Center under the auspices of the Western Institutional Review Board (WIRB), Seattle, Washington. All patients gave signed informed consent before participating in this research program. Patients receiving topical and/or systemic medications for treatment of their acne or those with a history of light-based treatments for their acne were excluded. Patient participants had a minimum of 15 facial inflammatory acne lesions, consisting of papules, pustules, and cysts, as determined by a board-certified dermatologist or registered nurse practitioner. All patients were more than 18 years of age and cleansed their faces with only Cetaphil™ liquid cleanser during the study.

Twenty patients received one ALA-PDT (with IPL activation) treatment per week for 4 weeks and returned for evaluation 4 and 12 weeks after the final treatment. Clinical photographs were taken and patients were questioned in detail for adverse effects during each treatment session and follow-up visit.

ALA (Levulan® Kerastick®, Dusa Pharmaceuticals, Inc., Wilmington, MA) was prepared and applied to the full face as described[16] and remained in contact with skin for one hour before removal with Cetaphil™ cleanser and treatment with IPL. Levulan® Kerastick® is shown in Figure 1.

IPL activation was accomplished with the SkinStation® (Figure 2, Radiancy, Inc., Orangeburg, NY), a table-top device with a ClearTouch™ system of two flash lamps that emit 430-nm to 1100-nm radiation at 3 to 9 J/cm^2 fluences. The SkinStation uses the proprietary LHE technology of both light and heat energy—light for the targeted indications (porphyrins and sebaceous glands) and heat to potentially stimulate further photodynamic reactions and to reduce inflammation. The SkinStation light pulse duration is 35 msec and the spot size is 22 x 55 mm. Treatments were administered at power settings throughout the 3 to 9 J/cm^2 range. Topical and/or systemic anesthesia was not used during the course of the project, nor any extra cooling devices.

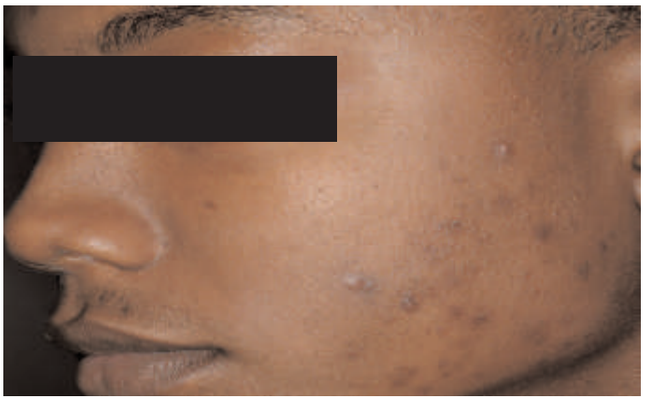

Figure 3a. Left cheek of a female patient shows inflammatory acne lesions before treatment with ALA (Levulan Kerastick) PDT and IPL (SkinStation) activation.

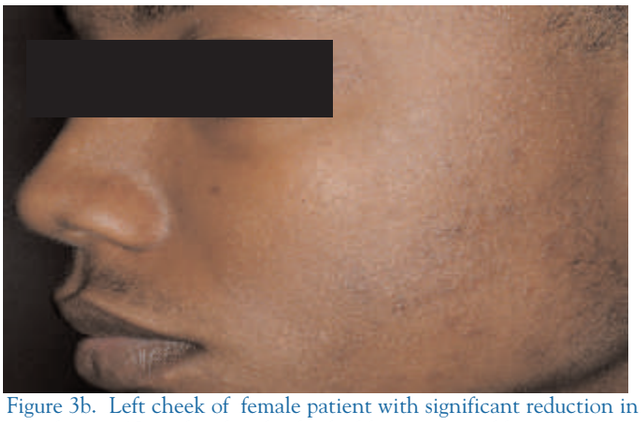

Figure 3b. Left cheek of female patient with significant reduction in acne lesions 12 weeks after the final of four once-weekly treatments.

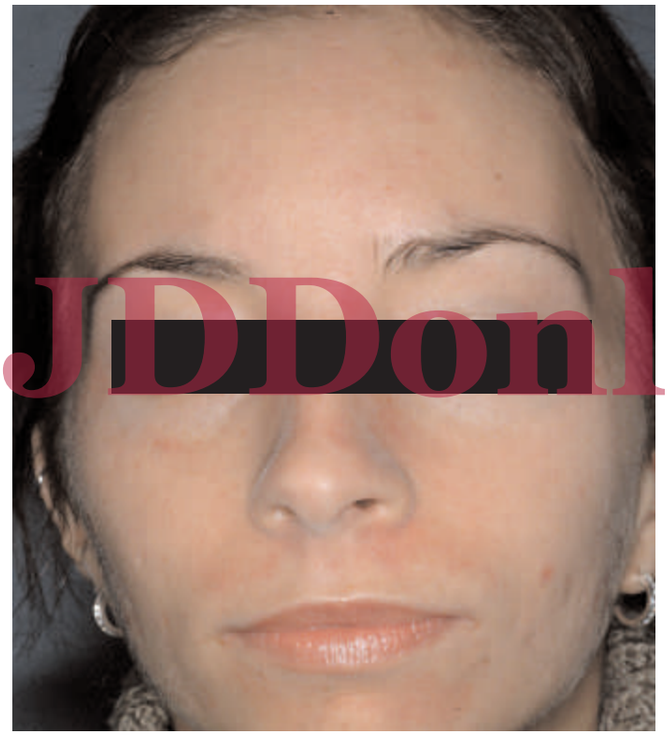

Figure 4a. Female patient with inflammatory acne lesions on forehead, nose, cheeks, nasolabial area, and chin before treatment with ALA (Levulan Kerastick) PDT and IPL (SkinStation) activation.

Figure 4b. Female patient with significant reduction in facial acne lesions 12 weeks after the final of four once-weekly treatments.

Figures 3 and 4. Patients reported no adverse events, recurrences, or changes during the treatment or follow-up periods.

Results

Fifteen of the 20 trial participants completed the study. Five patients were lost to follow-up during the clinical trial. Three (20%) did not respond to the treatment leaving 12 evaluable patients (10 women, 2 men) 20 to 54 years of age (mean 32.7 years).

Among these 12 patients, reduction in acne lesions was, on average, 50.1% at the end of the 4-week treatment period, 68.5% 4 weeks after the final treatment, and 71.8% 12 weeks after the final treatment. Clinical examples are shown in

Discussion

Our results show that ALA-PDT with SkinStation IPL activation is an effective and safe treatment for moderate to severe inflammatory acne vulgaris.

Early investigators[26-28] used a variety of light sources and long ALA incubation times to treat acne. In the first reported trial of ALA-PDT in the treatment of moderate to severe acne during a 22-patient study, Hongcharu et al[26] used 550- to 570-nm

broadband light to activate ALA incubated three hours. Significant clinical clearance was evident after four once-weekly treatments. Adverse effects included acneform folliculitis, post-inflammatory hyperpigmentation, superficial peeling, and crusting. Itoh et al[27] used ALA-PDT with 635-nm pulsed excimer-dye laser activation and 4-hour ALA incubation to treat a single patient with intractable acne vulgaris on the face. The treated area remained clear for at least 8 months. Classical PDT reactions—erythema, edema, and crusting—appeared after treatment. In a later study, Itoh et al[28] treated 13 patients with ALA-PDT, this time using 600-nm to 700-nm visible light from a less expensive halogen source. All patients showed improvement and new acne lesions were reduced at 1, 3, and 7 months after treatment. During the following 6 months, acne lesions reappeared and seborrhea returned in most patients. Again, erythema, edema, and crusting were evident after ALA-PDT.

Later investigators used blue light activation and shorter ALA incubation times. Goldman[29] treated acne and sebaceous gland hyperplasia with one-hour ALA drug incubation and either IPL or 15-minute blue light activation. Relative clearing of acne lesions occurred after 2 to 4 once-weekly treatments. Treatments were reported to be pain free and without adverse effects.

In a full-face study of 10 patients with moderate to severe acne, Gold[30] used 30- to 60-minute drug incubation time and high-intensity blue light activation once weekly for 4 weeks. Response rates averaged 60% with ALA-PDT compared to 43% with blue light alone. Treatments were well tolerated with no adverse effects.

Goldman and Boyce[31] treated 22 patients with moderate to severe inflammatory acne vulgaris with blue light with and without ALA photosensitizing agent. Blue light therapy was performed twice per week for 2 weeks with follow-up at 2 weeks; blue light plus ALA was performed two times at 2-week intervals with a follow-up at 2 weeks after the final treatment. There was a greater response in the ALA-PDT/blue light group than blue light alone with no significant adverse effects seen in either group of patients.

Concurrently, other investigators used blue light alone to treat inflammatory acne. Papageorgiou et al[9] reported a 63% response rate for inflammatory lesions and 45% for comedonal lesions, while Kawada et al[10] reported a 65% response rate for inflammatory lesions with blue light therapy. A high-intensity blue light source (ClearLight™, CureLight, Lumenis) has been shown to provide 60% to 75% improvement and a 20% average non-response rate in patients with acne[11,12]. Most of the trials described above used two treatments per week for 4 weeks with 1- and 3-month follow-up times.

In a study of 40 patients with mild to moderate inflammatory acne, Gold[13] obtained an average 43% improvement (including non-responders) with 4 weeks of twice-weekly treatments with a high-intensity blue light source. Patients were evaluated at 1 and 3 months after the final treatment. Improvement was maintained throughout the 3-month follow-up period.

Also FDA-cleared for the treatment of mild to moderate acne, the BLU-U® (Dusa Pharmaceuticals, Inc.), has been reported more effective than topical clindamycin (1%) in the treatment of inflammatory acne. Treatments were given over 4 weeks and patients were followed for 1 month[14].

Other investigators have used IPL for the treatment of acne vulgaris. Elmam et al[2] evaluated the ClearTouch™ acne clearance system. Eighty-five percent of their patients showed greater than 50% improvement in their acne lesions following a treatment regimen of bi-weekly treatments for 4 weeks and two follow-up visits after 1 and 2 months. Further improvement was observed at the 2-month follow-up, 85% versus 79%. Fifteen to 20% of the patients, however, were non-responders.

Gregory et al[17] reported similar results after a 1-month treatment phase and 1-month follow-up. In 75% of treated areas, a reduction in the number of inflamed lesions of 50% or more was achieved. The mechanism of action for IPLs is similar to that of blue light therapy except perhaps with an additional mode of action found – the radiation may attack and destroy the sebaceous glands themselves as well as destroying the P. acnes bacteria, leading to successful PDT[17].

Lasers are also effective against sebaceous glands. After preloading enlarged sebaceous glands with indocyanin green (ICG), Lloyd and Mirkov[15] directed 810-nm laser radiation at the ICG-loaded glands. Histological examination showed that the laser-treated glands had become necrotic and that acne in the treated areas had decreased at 3, 6, and 10-month follow-up visits. Longer wavelength laser radiation is also effective, as shown by the study of Paithankar et al[16] The authors showed histologically that 1450-nm laser radiation with cyogen cooling resulted in damage to the dermal layer containing the sebaceous glands with no damage to the epidermis of animal skin. They also showed that the same treatment reduced the lesion counts on the backs of human patients with few adverse effects. Recently, Friedman et al[34] demonstrated the usefulness of the 1450-nm diode laser on facial acne.

Our report further documents the effectiveness of lasers and light therapy on the treatment of moderate to severe inflammatory acne vulgaris. The SkinStation LHE source was shown to be an effective IPL light source in the group of patients we studied in the treatment of moderate to severe inflammatory acne. Our patients tolerated the procedure and the majority responded well to the therapy.

Overall, the combination of short-contact, full-face ALA-PDT with blue light, IPL, lasers, and other light sources appears to be effective against moderate to severe inflammatory acne. The

ALA-PDT combination is safe and appears to work faster than laser or light therapy alone. Fewer treatments are also required. In some patients, the combination may eliminate the need for more intensive systemic therapies.

Dr. Gold is a consultant for DUSA Pharmaceuticals, Inc. Dr. Gold performs research, speaks for, and owns stock in DUSA Pharmaceuticals, Inc. The SkinStation® LHE® from Radiancy, Inc., was loaned to Dr. Gold for use during the research project. Dr. Gold has no conflicts of interests with Radiancy.

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Case Report Winners Announcement

We are pleased to announce the winners of the Levulan Photodynamic Therapy (PDT) Case Report Competition. The Case Report Competition was made possible by an unrestricted educational grant from DUSA Pharmaceuticals, Inc. Entries describe treatment for therapeutic or cosmetic dermatologic cases using PDT. Cases must utilize Levulan® Kerastick® ALA (aminolevulinic acid HCl 20%) for topical solution.

The top five entries listed below will receive a Canon PowerShot 4.0 Megapixel Digital Camera Model A80. The top two entries, published in full to follow, will receive full registration to the Second Annual Orlando Dermatology and Cosmetic Conference to be held January 14-17, 2005, in Orlando, Florida in addition to the digital camera.

We would like to thank everyone for their submissions.

1. Laser-Mediated Photodynamic Therapy of Lichen Sclerosus by Macrene Alexiades-Armenakas, MD, PhD
2. Red Light Laser Photodynamic Therapy of Bowen's Disease by Eric C. Parlette, MD
3. Use of Photodynamic Therapy to Treat Unilateral Basal Cell Carcinomas by Joshua E. Lane, MD, Jennifer H. Allen, MD, and Jack L. Lesher, Jr., MD
4. Broad Area Photodynamic Therapy for Treatment of Multiple Basal Cell Carcinomas in a Patient with Nevoid Basal Cell Carcinoma Syndrome by Anne M. Chapas, MD, and Barbara A. Gilchrest, MD
5. Photodynamic Therapy in Erythema, Papules, Pustules and Severe Flushing by Vikas Patel, MD

Red Light Laser Photodynamic Therapy of Bowen's Disease

Eric C. Parlette MD LCDR MC USNR

Dermatology Department, Naval Medical Center, San Diego, CA

Case Report

A 68-year-old white male presented with a history of a slowly enlarging erythematous plaque on his left posterior upper arm over the past 7 years. On physical examination, the patient had a 4-cm erythematous, finely scaling, well-demarcated plaque on his left posterior, mid upper arm (Figure 1). Biopsy of the lesion confirmed a diagnosis of Bowen's disease (Figure 2). Given the extensive size of the lesion and location, we opted to treat the patient with photodynamic therapy with topical aminolevulinic acid.

Day one, the patient presented for application of the aminolevulinic acid hydrochloride 20% (ALA) solution at 2:35 pm. The entirety of the contents from a Levulan® Kerastick® (ALA), 350 mg, was topically applied to the plaque of Bowen's disease on the patient's left posterior upper arm. The plaque was then occluded with a completely opaque dressing (Figure 3). He was instructed to keep this area dry and out of the sun until follow-up the next day at 8 am.

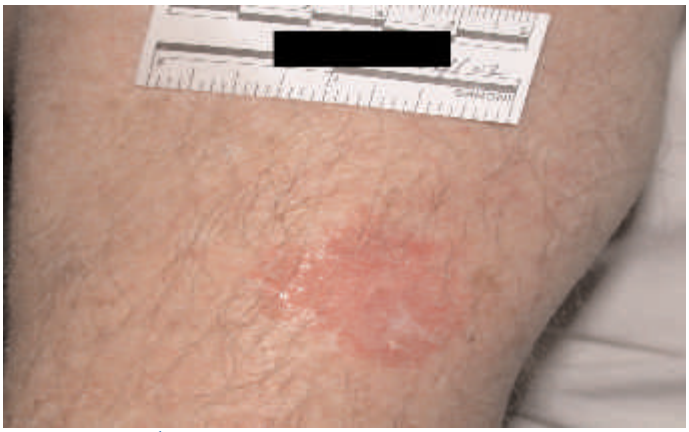

Figure 1. Initial examination.

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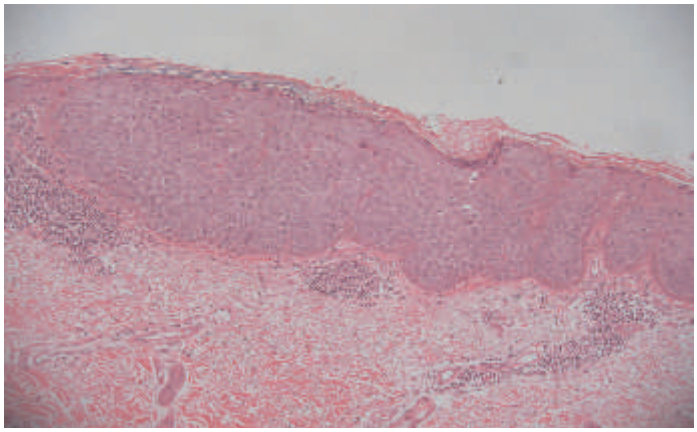

Figure 2. Biopsy of lesion.

Day two, the patient returned for follow-up and photodynamic therapy (PDT) using a 630-nm dye laser. A prescribed light dose of 150 Joules/cm^2 was calculated. The PDT calibrated output power was 2.98 Watts. The treatment area was 12.57cm^2. Dose rate being equal to output power/treatment area was

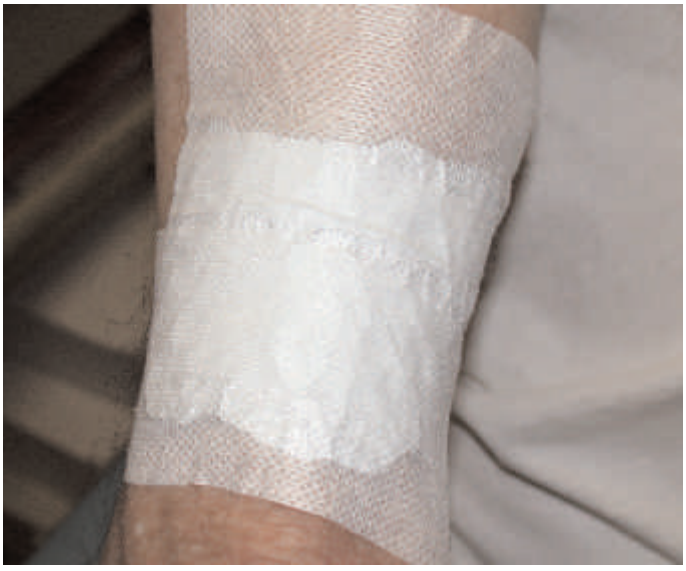

Figure 3. ALA occluded.

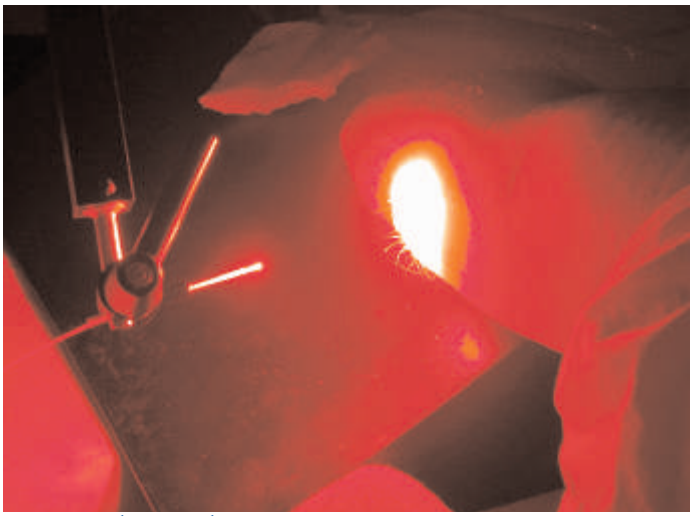

Figure 4. The procedure.

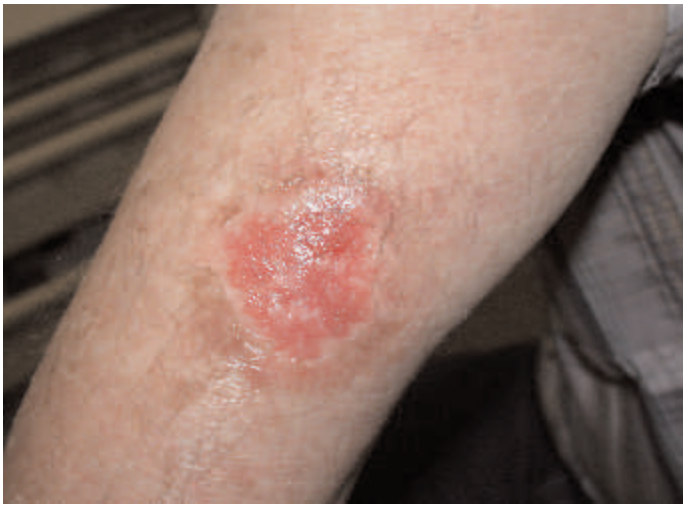

Figure 5. Two weeks out.

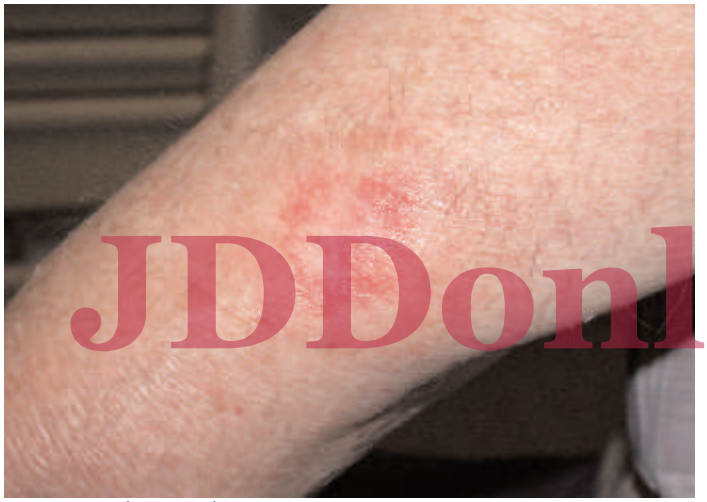

Figure 6. Three weeks out.

Figure 7. One month out.

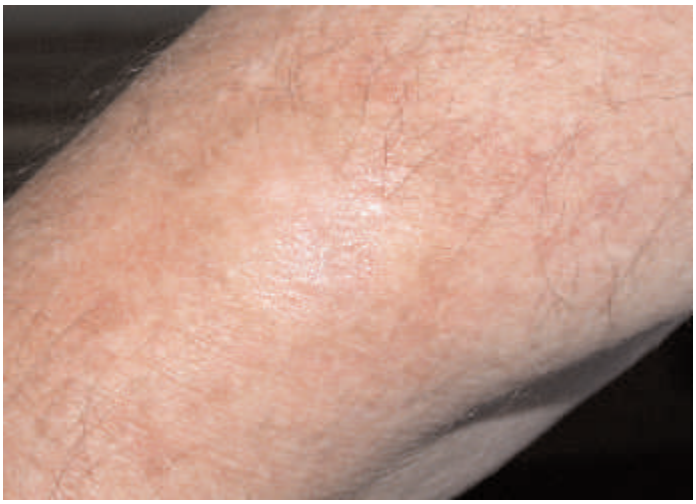

Figure 8. Three months out.

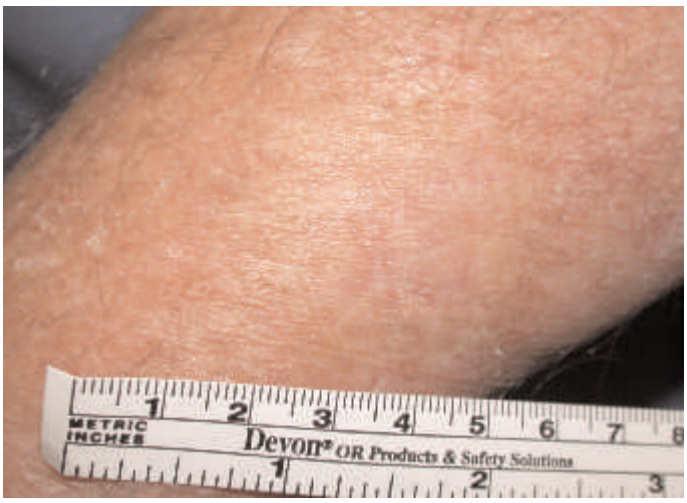

Figure 9. Two years two months out.

0.237W/cm^2. The treatment time, light dose/dose rate, was determined to be 632 seconds (10.5 minutes).

The ALA was left in place for a total of 18 hours, 25 minutes before treatment. The area was locally anesthetized using 9cc of 2% lidocaine with epinephrine. A 630-nm dye laser was then used to activate the protoporphyrin IX. The perpendicular treatment distance was 7.0 cm with a treatment area of 12.57cm^2 and field diameter of 4.0 cm (Figure 4). The patient remained motionless during the course of the procedure without any discomfort. The patient noted significant aching in the treatment zone over the next 18 hours which was relieved with oral narcotics. This quickly resolved and was subsequently asymptomatic for the remainder of the healing process.

At 2 weeks follow-up, the treated plaque was erythematous and still appeared to be significantly inflamed (Figure 5). One week later, at 3 weeks, the erythema and inflammation had substantially subsided (Figure 6). At 1 month, there was very trace erythema in the treatment zone with focal alopecia of the entire area (Figure 7). At two and a half months follow-up, there was no clinical evidence of tumor, only persistent alopecia (Figure 8). The patient remains disease free at over 2 years follow-up (Figure 9). There is still complete alopecia involving the entire 4-mm treatment area. The alopecia supports the fact that topical ALA photodynamic therapy with 630-nm dye laser effectively treats down to the level of the follicular epithelial atypia seen in Bowen's disease.

Laser-Mediated Photodynamic Therapy of Lichen Sclerosus

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Case Report

Patient: J. F., 67-year-old woman

Duration: Three years

Distribution: Shoulders, axillae, and abdomen

History

The patient presented with a 3-year history of mildly itchy lesions developing on her abdomen, shoulders, and underarms. An outside dermatologist told her that she had psoriasis, and she was treated with a mild cortisone cream without improvement. When she presented to the author's private practice, a skin biopsy was performed, which demonstrated lichen sclerosus.

Physical Examination

Multiple large, well-demarcated, erythematous plaques with porcelain-white and parchment-like atrophy, and superimposed thin, white scales were distributed on the shoulders, axillae, and abdomen. Initial examination: Erythema 3, Scale 2, Atrophy 3 (Figure 1).

Treatment

The various treatment options for her condition were discussed including topical and intralesional corticosteroids, topical estrogen and testosterone preparations, keratolytics and retinoids, and the most recent advent of photodynamic therapy. She opted to pursue photodynamic therapy, understanding that this approach had only one prior report in the literature and was not FDA-approved for this condition. Verbal and written consent was obtained.

The lesions were allocated to receive topical 20% 5-aminolevulinic acid (ALA) HCl solution (Levulan®, DUSA pharmaceuticals) followed by long-pulsed dye laser (LP PDL) (treatment) versus LP PDL alone (control). Topical 5-ALA was applied as described in the manufacturer's instructions for a 1-hour incubation time to the designated areas. This was followed by two passes with minimally overlapping pulses of LP PDL (595 nm, V beam laser, Candela, Wayland, MA) irradiation at 7.5 J/cm^2 fluence, 10 ms pulse duration, 10 mm spot size, and dynamic cooling spray at 30 ms with a 30 ms delay to both the ALA-treated and untreated lesions. Three treatment sessions were performed at 1-month intervals.

Figure 1. Initial examination.

Patient Progress

1. ALA-LP PDL treated lesions: Following ALA application, the patient reported no stinging, burning or discomfort. During laser-irradiation, she reported absent-to-slight pain or discomfort. Immediately following treatment, the areas were mildly

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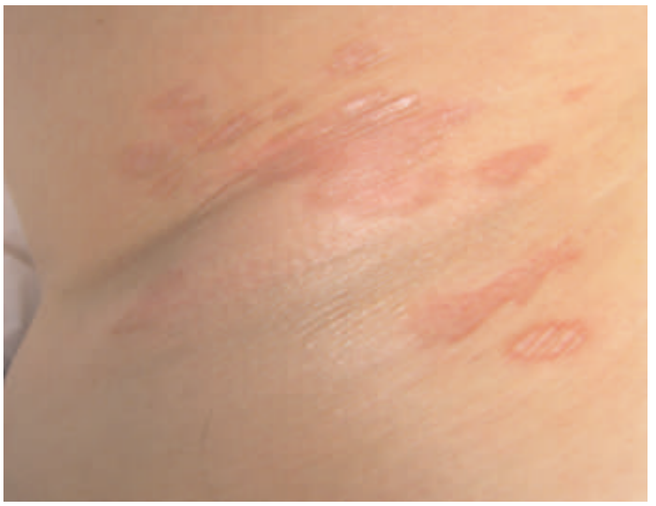

Figure 2. Immediately following first treatment. (The lesion on the lower right is the control lesion.)

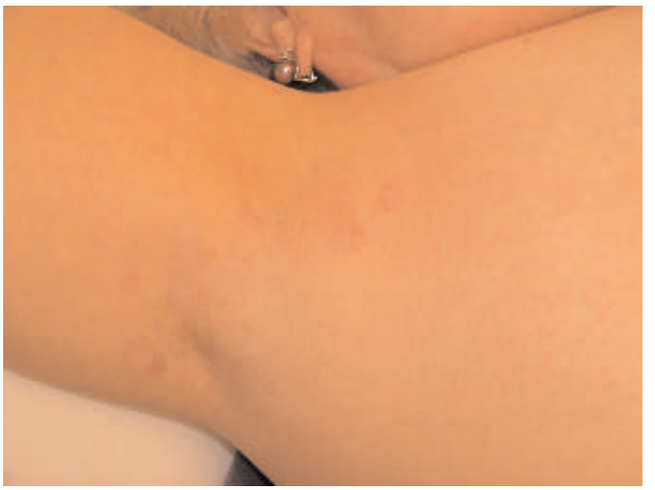

Figure 3. At 1 month after 3 treatments. (The lesion on the upper right is the control lesion.)

erythematous and the patient reported absent-to-slight stinging to the treatment areas (Figure 2). Erythema resolved in 3 days.

Following each treatment, a progressive improvement in the appearance of the lesions was observed. At the 1-month follow-up interval following 3 monthly treatments, assessment revealed: Erythema 1, Scale 0, Atrophy 0 (Figure 3). The patient reported resolution of the associated pruritus.

2. LP PDL only, control lesions: During laser-irradiation, the patient reported absent-to-slight pain or discomfort. Immediately following treatment, the control areas were slightly erythematous and the patient reported no stinging or discomfort. Erythema resolved within hours (Figure 2).

Following each treatment, slight improvement in erythema was observed, but no change in scaling or atrophy. At the 1-month follow-up interval following 3 monthly treatments, assessment demonstrated: Erythema 2, Scale 2, Atrophy 2 (Figure 3). The patient reported persistence of pruritus to control lesions.

Comment

Lichen sclerosus (LS) was first described by Hallopeau in 1887 as lichen plan atrophique and has since been variously termed lichen sclerosus et atrophicus, balanitis xerotica obliterans, and kaurosis vulvae[1]. It most commonly involves the vulva and perineum of women, and the penis and foreskin of males[2]. Approximately 20% of patients are estimated to possess extragenital lesions, which most commonly present on the neck and shoulders[3]. The condition affects children in 10% to 15% of cases and most of these cases involve the female genitalia. The remaining cases involve adults, most commonly females with a ratio of 10:1 relative to males. The symptoms of genital LS include pruritus, burning, dyspareunia, dysuria, discharge, bleeding, labial stenosis, and constipation in women, and phimosis, adhesions, decreased sensation, painful erections, dysuria, discharge, and urinary obstruction in men. Extragenital LS is associated with occasional pruritus. The Koebner phenomenon has been observed following surgical procedures, trauma, and scars[2]. The prognosis of LS is that of a chronic condition, with waxing and waning symptoms and only occasional spontaneous remissions. Spontaneous resolutions have occurred primarily in menarchal girls.

Major complications of LS include phimosis, labial stenosis, and malignancy. LS was responsible for 22% of phimosis cases among boys ages 5 to 11 in one series[4] and 60% in another[5]. Labial fusion and resorption can occur, decreasing the size of the introitus and resulting in marked dyspareunia[6]. Of great import, premalignant and malignant transformation may occur in patients with LS, with estimates as high as 50% demonstrating such changes[6]. Squamous cell carcinoma developed in 4.4% of vulval LS in one series[7]. In another study, 68 (33%) cases of LS were identified among 207 penectomy and circumcision specimens for SCC[8]. SCC has also reported among cases of juvenile LS[3]. Patients with LS need to be monitored every 6 months in order to screen for the development of carcinoma.

The etiology of LS as an autoimmune disease has recently been elucidated. Clinicopathological similarities between LS and the congenital disorder lipoid proteinosis, which is due to mutations in extracellular matrix protein 1 (ECM1), and HLA-subtype susceptibility among LS patients suggested to John McGrath and colleagues that ECM1 was an autoantigen. Autoantibodies of the IgG type were subsequently found directed against ECM1 in 67% of LS patients as compared to 7% of controls[9]. These data provided strong evidence for a specific autoimmune response to ECM1 in LS. Thus, modulation of the autoimmune response in the skin and the superficial sclerotic

changes that ensue would be the ideal form of treatment of this disease.

Prior treatments have included principally high potency topical glucocorticoids, clobetasol reproducibly demonstrating the best results[10]. Intralesional corticosteroids, keratolytics, and antihistamines have also been helpful in combination with topical therapy. Topical estrogen has been variably effective in the treatment of vulvar and penile LS. Topical testosterone has been reported to be highly beneficial, though this author has not achieved much success with this modality. Topical progesterone has been reported to show modest efficacy. Retinoids, when given orally, result in notable improvement, but topically are not well-tolerated due to irritation[11]. Recently, topical tacrolimus and pimecrolimus have been utilized[12].

Photodynamic therapy was reported in one prior case report for the treatment of genital LS. Twelve women with vulvar LS were treated with one to three sessions of topical 20% 5-ALA followed by argon ion-pumped dye laser at 635 nm[13]. A decrease in pruritus was reported in 10 of 12 women for a mean duration of 6 months. In another study, 12 patients with genital LS were treated with topical PUVA, which resulted in clinical improvement after 10-20 treatments[14]. A preliminary study has suggested possible benefit from UVA1 phototherapy[15].

This is the first report of ALA-PDT with LP PDL for extragenital LS. A significant improvement in the erythema, scaling and atrophy as well as resolution pruritus was demonstrated after 3 monthly treatments. A marked difference was observed between the ALA-PDT treated lesions and the LP PDL-only controls. The mechanism of PDT in conjunction with LP PDL in this case may involve modulation of the autoimmune response in the skin and possible upregulation of superficial collagen formation. Potential hypotheses include that the PDT targets include the papillary blood vessels, which are necessary for trafficking of lymphocytes, and/or activated lymphocytes directly. Alternatively, the PDT LP PDL response may upregulate collagen formation by fibroblasts and more effectively diminish the pathologically dilated blood vessels than LP PDL alone. The potential advantages of this approach include the rapid treatment and recovery times, relatively few treatments as compared to other modalities, and the avoidance of systemic toxicity for this autoimmune disease.

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