Standardization Comes to PDT

Guidelines *from page 1*

on what works and what doesn't work, everyone has a problem getting confused. Somebody gets results, and somebody doesn't," he said at the conference, which was sponsored by the Center for Bio-Medical Communication Inc.

Botox pioneers Dr. Alastair Carruthers and Dr. Jean Carruthers were among 13 board members of the American Society for Photodynamic Therapy who joined the consensus panel in signing the guidelines. Dr. Nestor, society president, said it will announce its first meeting later this year.

The experts agreed that PDT using topical 5-aminolevulinic acid (ALA) has "significant promise in improving the clinical and cosmetic outcomes of patients with a variety of cutaneous conditions."

Nonetheless, despite Food and Drug Administration clearance of two photodynamic devices—the Levulan Kerastick in 1999 and the BLU-U Blue Light Photodynamic Therapy Illuminator in 2000—PDT has not been widely adopted, according to the panel.

It suggested four reasons for the slow pace: the fact that the ALA indication is limited to treatment of nonhypertrophic actinic keratoses of the face and scalp, concerns about patient "downtime" and photosensitivity, poor reimbursement, and lack of clinical guidelines.

PDT is safe and effective for a variety of dermatologic conditions, the panel said, concluding that "the expanding clinical and financial benefits of ALA-PDT justify the purchase of an appropriate light source."

The panel calculated that 94% of patients who participated in phase III trials of actinic keratoses rated their cosmetic outcomes as good to excellent. Additionally, the authors cited evidence that PDT with ALA might be an alternative to 5-fluorouracil for treating multiple actinic keratoses over large skin surfaces.

The panel outlined treatment criteria for three categories of photoaging:

► **Photodamage type A.** "Superficial changes in complexion, including vascular and pigmentary changes, lentigines, telangiectasias, erythema, symptoms of rosacea, and melasma" should be treated with intense pulsed light (IPL) alone or in combination with topical treatments.

► **Photodamage type B.** "Structural changes in the dermis and epidermis resulting in rhytides, large pores, lax and actinically damaged skin" should be treated with IPL in combination with 1064-nm, 1320-nm Nd:YAG laser.

► **Photodamage type C.** "Severe elastosis associated with actinic keratosis, early skin cancer, type A damage, type B damage" should be treated by ALA-PDT with IPL.

The guidelines also make several other recommendations:

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Preventing Cancer

Treating nonmelanoma skin cancers with photodynamic therapy may prevent a substantial number of skin cancers from developing, according to Dr. Nestor.

He said he followed five patients with active facial nonmelanoma skin cancer for 5 years. From 2001 to 2003, they averaged about five new skin cancers per patient per year. After photodynamic therapy in 2003, the number of new skin cancers fell by 80% to one per year.

"We see dramatic improvement in overall sun damage, but we should not just look at improvement," he said at the conference.

"I look at this as chemoprevention," he said. "This would be nice to see as we go forward. This, in and of itself, is very exciting."

Photodynamic Therapy's Efficacy Draws Strong Testimonials

BY BETSY BATES
Los Angeles Bureau

LOS CABOS, MEXICO — Advances in photodynamic therapy (PDT) using 5-aminolevulinic acid (ALA) have led dermatologists to increasingly extol its virtues as a practical, versatile, and highly effective therapy for actinic keratoses, nonmelanoma skin cancer, acne, and photorejuvenation.

For example, at the annual meeting of the Noah Worcester Dermatological Society, several dermatologists described ALA-PDT with a degree of enthusiasm pointedly absent from presentations concerning many new lasers, skin smoothers, and nonablative, all-purpose devices.

"[It has] … changed the way I practice," Dr. C. William Hanke said at the meeting.

Dr. Hanke said he recalled hearing about ALA-PDT at an American Academy of Dermatology meeting 5 years ago. His impression of the therapy then was "how terrible it was. There was a lot of handholding … because the patient needed it."

Still, it seemed to work pretty well in eradicating actinic keratoses (AKs), and a 2003 study showed that it had the potential to be equal to 5-fluorouracil in efficacy and was preferred by most patients, despite the painful recovery required after a 14- to 18-hour ALA incubation period and subsequent exposure to a specialized light source (J. Drugs Dermatol. 2003;2:629-35).

Since then, ALA-PDT has changed dramatically in the following ways:

► **Short-contact ALA-PDT is now standard.** ALA remains on the skin just 15-60 minutes, profoundly affecting the side-effect profile and reducing pain. Instead of enduring a week of raw skin, erosions, and inflammation, most patients today note only minor stinging, erythema, and scaling that resolve within a few days. Many studies show that short-contact ALA-PDT does not reduce its effectiveness.

► **Numerous light sources are being used.** Although blue light emits a wavelength (405-420 nm) that conforms precisely to the absorption peak for ALA (marketed as the Levulan Kerastick by DUSA Pharmaceuticals Inc.), intense pulsed light (IPL), pulsed dye lasers, and other light sources also are proving effective.

► **The versatility of ALA-PDT is expanding.** Approved for nonhyperkeratotic AKs of the face and scalp, it also is being used on the trunk and extremities for AKs, nonmelanoma skin cancer, pigmented lesions, rosacea, and, especially, acne.

► **Competition is on the horizon.** An American launch is imminent for the photosensitizer methyl aminolevulinate, marketed as Metvix by the Norwegian company PhotoCure ASA. Widely used in Europe, Metvix is incubated for 3 hours under occlusion and activated by red light (630-660 nm) from a diode laser. Besides treating AKs and nonmelanoma skin cancer, the system is used to treat psoriasis.

Dr. Neil S. Sadick voiced a common complaint when he noted that nonablative therapies have now been used for 5 years to treat everything from rosacea to scars, "and we're still not sure [they're] effective or worth it."

In contrast, he said that IPL, which targets chromophores, has become a mainstay in his practice, "providing the greatest amount of clinical satisfaction, consistently, for [the] patients."

When he's treating more than telangiectasias, age spots, and minimal actinic damage, Dr. Sadick said he relies on ALA to amplify the impact of IPL.

"I can decrease five treatments to two [or] three treatments with IPL … for significant actinic damage. It's not nonablative; I would call it microablative," said Dr. Sadick, who practices in New York City and Great Neck, N.Y.

Dr. Mitchel P. Goldman said short-contact ALA-PDT using IPL is "incredibly impressive" for acne and a convenient and "very mildly painful" option for patients with actinic keratoses, telangiectasias, and skin texture problems. He even used the modality to treat his own facial squamous cell carcinoma.

He uses a pulsed dye laser rather than IPL on hair-bearing areas because IPL can remove hair.

Like Dr. Sadick, Dr. Goldman uses ALA-PDT to "boost" the effectiveness of IPL, reducing the number of treatments required.

After one or two treatments of ALA-PDT with IPL for actinic keratoses, "I think that's when you need to biopsy," said Dr. Goldman, who is in private practice in La Jolla, Calif.

Dr. Hanke, director of a dermatologic surgery practice in Carmel, Ind., says that ALA-PDT has become ever more useful in his practice over time, for cosmetic as well as medical dermatology.

If a patient's goal is to have smoother, clearer skin, with less blotchiness and redness, "we can do that," he said.

There are conditions, such as wrinkles, that do not respond well to ALA-PDT, the speakers agreed. In addition, Dr. Hanke said he was unimpressed by its results in a renal transplant patient with extreme sun damage that included a history of skin cancers and many keratoses.

It also doesn't work for disseminated superficial actinic porokeratosis or granulomatous rosacea, he concluded.

Its record in treating warts is erratic, he said, although he has had luck sometimes by paring the wart down, applying several coats of ALA, and then occluding the wart overnight prior to exposure to a light source.

Dr. Hanke has conducted clinical trials for DUSA Pharmaceuticals. Dr. Goldman has been a consultant for DUSA and for the Luminis LightSheer diode laser system, which can be used for phototherapy. Dr. Sadick has conducted research and/or consulted with Syneron, Thermage Inc., and Omnilux Inc., companies that manufacture lasers and light sources that can be used in phototherapy. ■

Getting the Most from PDT

The following steps can maximize the effects of ALA-PDT:

1. Discontinue topical retinoids several weeks before treatment with 5-aminolevulinic acid photodynamic therapy (ALA-PDT).
2. Prepare the skin using gentle microdermabrasion or acetone (to maximize the PDT reaction), or isopropyl alcohol (to minimize the PDT reaction).
3. Use a fresh ampule of Levulan Kerastick (ALA). The drug becomes inactive 4 hours after being opened.
4. Apply two coats of ALA with a cotton swab. Take extra care to avoid getting the solution in the patient's eyes.
5. Adjust exposure to ALA and to the light or laser source according to the patient's condition and severity. For example, the photosensitizer should remain on the skin 60 minutes prior to PDT for treatment of photoaging. Exposure time will vary: 22-25 minutes for an intense pulsed light source or 16 minutes and 40 seconds for a blue light source.
6. Use cool airflow, rest periods, and, possibly, topical anesthesia or diazepam (5-10 mg) for pain management.
7. Observe the patient post phototherapy, and wash the area thoroughly with soap and water to ensure that all of the photosensitizer has been removed. Apply sunscreen in the office.
8. Be adamant in instructing the patient to avoid sun exposure altogether for 24 hours and to wear heavy sunscreen for 3-4 days. Patients can have extreme reactions to sun exposure in the days following phototherapy.

Source: Dr. Hanke