PDT resurfaces as latest skin rejuvenation treatment

BY EMMANUELLE BASSMANN / POSTED IN DERMATOLOGY ON JANUARY 16, 2014

With photodynamic therapy approved by the FDA to treat skin lesions since 2004, Emmanuelle Bassmann discusses whether it is still the number one treatment for skin cancer, and considers its off-label uses such as acne and rejuvenation

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- Using LED photobiomodulation to treat premature ageing

LEONARDO MARINI / MARCH 4, 2013

Over the past 25 years, photodynamic therapy (PDT) has been useful in the treatment of skin cancer lesions. It is a two-step treatment consisting of topical delivery of photosensitising drugs 5-aminolaevulinic acid (ALA) or methyl aminolaevulinate (MAL), followed by light irradiation to destroy tumour cells. It is a simple treatment: dermatologists apply the photosensitising agent topically, which needs to sit on the skin for 3 hours before a red or blue light is irradiated on the skin.

PDT remains the treatment of choice to treat basal cell carcinoma (BCC; a form of non-malignant skin cancer) and actinic keratosis (AK, or pre-cancerous skin lesions), and is quickly gaining recognition treating Bowen's disease, a very early form of squamous cell skin cancer.

According to international guidelines published in the January 2007 issue of the*Journal of the American Academy of Dermatology*[1], PDT has been recommended by a consensus group of physicians as a highly effective first-line treatment for AK.

Available PDT treatments

Two leading drugs are available on the market today: MAL–PDT with Metvix® (Galderma Laboratories, LP., Ft. Worth, TX) and ALA–PDT with Levulan® (DUSA Pharmaceuticals, Wilmington, MA). The differences are set out in a study published in the *Journal of Clinical and Aesthetic Dermatology* in February 2009, by Dr Michael H. Gold[2].

MAL

Metvix has been successfully used for the treatment of skin cancer for a long time in Europe and other places around the world, including Australia, Brazil, and some parts of Asia. It comes as either a 20% 5-ALA solution or a methyl ester cream (MAL). It has now been approved for the treatment of BCC and AK in over 30 countries, including the EU, Australia, New Zealand, and Brazil. Metvix and the LED emitting lamp Aktilite® (Galderma Laboratories, LP.) were also recently recognised for the treatment of Bowen's disease in 22 European countries. In the US, Metvix/Aktilite were only approved for AK in 2008. MAL is best used with a red light source at 630 nm. The recommended use of MAL requires lesion preparation prior to drug incubation and light exposure, where the lesions are prepared with a gentle curettage, followed by 3-hour drug incubation under an occlusive film or dressing to enhance the penetration of the drug. Light exposure, in the form of red light, is given after this 3-hour drug incubation period.

ALA

Levulan Kerastick™ (DUSA Pharmaceuticals, Inc.) is the commercial name for ALA. The Levulan Kerastick™ is a 20% weight/volume 5-ALA solution with 48% alcohol. It has a special, roll-on, dermatologic applicator at one end to allow easy and accurate application of the medicine.

In the US, the primary indications for the use of Levulan include the treatment of AK with or without a photorejuvenation effect, moderate-to-severe inflammatory acne vulgaris, sebaceous gland hyperplasia, and hidradenitis suppurativa. Levulan also has FDA clearance for the treatment of non-hyperkeratotic AK of the face and scalp. While it is more commonly used in the US for the treatment of AK, in South America and Asia its predominant use appears to be in the treatment of moderate-to-severe inflammatory acne vulgaris. Levulan Kerastick™ system comes with its own light source. In 2000, the FDA approved Berlex Laboratories and DUSA Pharmaceuticals' BLU-U® Blue

Light Photodynamic Therapy Illuminator (Wilmington, MA), which is used exclusively in the Levulan PDT for treatment of AK of the face or scalp. Clinical studies have shown that 8 weeks after beginning treatment with Levulan Kerastick™ and BLU-U, approximately 80% of patients reported 75% or more of their treated AK as completely clear (could not be identified by sight or touch)[3].

Pre-PDT steps for greater penetration

Pre-PDT treatments to enhance penetration of topical drugs are a growing trend, with many physicians developing their own methods to boost the penetration of the key active 5-ALA. A very simple and quick method is derma-sanding with sterile sand papers.

Fractional laser-assisted PDT

The use of fractional lasers to intensify the function of PDT, such as intensified ablative fractional laser-assisted photodynamic therapy (AFXL–PDT), is rising.

Dr Merete Haedersdal of the University of Copenhagen uses AFXL-PDT in high-risk populations such as organ transplant recipients (OTRs). Dr Haedersdal was one of the contributing authors of a study published in the June 2013 issue of the*British Journal of Dermatology*[4], which compared the use of intensified fractional carbon dioxide (CO_2) laser-assisted PDT and laser therapy alone for OTRs with multiple actinic keratoses and wart-like lesions. The study found that OTRs are at a 100-fold or greater risk of developing squamous cell carcinomas, which can arise from AKs, because of their chronic immunosuppressive treatment regimens. OTRs often develop multiple AKs in chronically sun-exposed areas, representing skin areas with field cancerisation. AFXL intensifies the PDT response and may improve the efficacy of AK clearance. AFXL–assisted PDT is more effective than AFXL alone in the treatment of acral AK in OTRs. It's possible that non-ablative fractional laser pre-PDT might also work (a new study has been published in the *British Journal Of Dermatology*[5]). According to Dr Haedersdal, AFXL-PDT could also be a potential treatment for skin rejuvenation but it is important to reduce the incubation time for the use of the photosensitiser, or the patient runs the risk of heavy skin reactions post treatment.

Dr Leonardo Marini of the Skin Doctors Center of Trieste, uses advanced thermo-fractional ablative PDT with a fractional ablative laser (2940 nm Erbium:YAG or 10600 nm CO_2) to increase the penetration of the photosensitiser up to 7.8-times (fractional priming) during the preparation phase. During the activation time, he uses a triple LED irradiation strategy preceded by a super-long 1064 nm Nd:YAG laser to increase the skin temperature to improve the conversion of 5-ALA into protoporphyrin IX (PpIX). However, Dr Marini warned that the use of this treatment during the summer months needs to be monitored more carefully as the risks for post-inflammatory hyperpigmentation (PIH) with advanced thermo-fractional ablative PDT are greater .