

## A Review Of Photodynamic Treatment In Dermatology

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### ABSTRACT

Skin cancers other than melanoma can be prevented and treated with photodynamic therapy (PDT). Clinically approved indications were previously limited to Bowen disease since 2006, nodular and superficial basal cell carcinoma, and actinic keratoses. The variety of signals has, nevertheless, been steadily growing. PDT is also used to treat leishmaniasis and other non-malignant disorders including acne vulgaris, as well as to delay the signs of premature ageing brought on by sun exposure. The concentration and localisation of the photosensitizer in the diseased tissue, as well as the light dose given, all affect the generation of reactive oxygen intermediates like singlet oxygen.[1-2] Either immunomodulatory effects that improve inflammatory skin conditions or cytotoxic actions that destroy tumours are induced. PDT has been demonstrated to be quite effective in treating superficial non-melanoma skin cancer despite its low degree of invasiveness. The outstanding cosmetic outcomes following treatment are also advantageous.

**Keywords:** Photodynamic therapy (PDT), Porphyrins, Actinic keratosis (AK). Light emitting diode (LED)

### Definition of PDT

In photodynamic therapy, a photosensitizer is activated by visible light to produce free radicals and cytotoxic oxygen species that specifically kill rapidly reproducing cells [6,7]. Where the size, location, or number of lesions restrict the efficacy and/or acceptance of traditional therapy, PDT may be helpful.

### **Mechanism of action**

The fundamental of photodynamic therapy is a multi-step procedure. In the first step, a photosensitizer must be applied topically or systemically in the absence of light. This drug has a very low dark toxicity. After the target disease's optimal ratio of photosensitizer to healthy cells is established, the diseased tissue is exposed to a precisely controlled dosage of light for a predetermined period of time that corresponds to the amount of energy required to activate the photosensitizer.[1-4]

It is important to take precautions to keep the energy at a level that is safe for the nearby healthy tissues. When the photosensitizer is activated, photochemical processes are triggered that result in the production of poisonous substances that are fatal, like reactive oxygen species.[5,8] These harmful radicals cause tissue deterioration and cell death. The extended accumulation of photosensitizer in sick cells and the quick removal from normal tissue cells are the cornerstones of the effective application of PDT & Photosensitizers: Photofrin was the first photosensitizer to receive regulatory approval for clinical PDT, but second- and third-generation photosensitizers were studied due to a number of its drawbacks, including prolonged patient photosensitivity. The second generation photosensitizers have enhanced selectivity and activity and are typically single compounds rather than necessarily porphyrins. By covalently attaching to monoclonal antibodies, for instance, the third generation photosensitizers include an additional targeting mechanism.

In order to optimise a treatment regimen based on typical skin fluorescence measurements, Christiansen and colleagues [8] published a study in 2007. The liposomal vehicle was preferable because it allowed the ALA to attain maximum fluorescence at concentrations of 0.5% and 1%

in just 2 hours, whereas the ALA in the cream vehicle required nearly 8 hours and a far greater concentration of 20% to obtain the same results.

### **Lasers in PDT**

To address skin conditions, light and chemicals are frequently combined. PDT was first introduced for this use's primary branch. PDT is a promising treatment option for non-malignant skin conditions and malignancies.[9]

Its foundation is the injection of a photosensitizer that localises specifically in the target tissue. Photodamage and consequent tissue loss occur when the lesion is exposed to visible light while still being in the presence of oxygen [10].

Lasers were used in medicine not long after their creation in 1960. The fundamental properties of laser light, such as coherence and monochromaticity, made them suitable tools for a variety of uses, including surgery, the treatment of hemangiomas, skin renewal, hair removal, etc. [11]. This feature is not required for PDT because coherence is lost within a few tenths of a millimetre upon penetration into human tissue. As a result, neoplasms are frequently exposed to non-coherent light. The output properties of non-coherent light sources are fundamentally different from those of lasers. PDT has been performed using lasers and non-coherent light sources, which typically exhibit comparable efficacies [12].

Non-coherent light sources are reasonably priced, stable, simple to use, and low maintenance. Larger bandwidths of light are frequently emitted by noncoherent, filtered light sources than by lasers and LEDs. It is difficult to compare two similar light sources, for this reason. Dosimetric considerations must be made carefully [13].

Pulsed dye lasers and diode lasers are frequently utilised for PDT. 21 patients underwent treatment with a 20% ALA solution followed by activation with LP PDL in a research evaluating the safety and effectiveness of the long-pulsed pulsed dye laser (LP PDL) (595 nm) with PDT for the treatment of actinic cheilitis (AC) [18]. Of these, the illness was resolved in 37% after just

one treatment, 68% after 1.8 treatments, and 21% after three. Impetiginization developed postoperatively in three patients with erosive AC.

The flashlamp pumped pulsed dye laser and the filtered flashlamp/intense pulsed light are two pulsed light sources used to treat various elements of cutaneous photodamage (IPL). Recently, ALA and these have been combined to treat photodamage. IPL and PDL had a weak dose-response effect on PDT activation, but Strasswimmer and Grande [19] showed that they were less effective than a weaker fluence of CW blue light.

### **Dermatological applications/indications**

Actinic keratoses are now the only indication for ALA PDT and MAL PDT that the Food and Drug Administration (FDA) has approved. The treatment of basal cell carcinoma (BCC), photo-aging, acne vulgaris, Bowen's disease, and hidradenitis suppurativa are among the off-label and alternate uses.

A full response rate of 92% for superficial BCCs and 71% for nodular BCCs with ALA PDT was reported by Zeitouni et al. in 2001 [10]. Numerous studies have been conducted to evaluate the efficacy and safety of PDT treatment for a variety of purposes.

### **Uses**

Atopic keratosis Epithelial skin malignancies account for more than 90% of all neoplasias in transplant recipients [21].vulgar acne Due to the increase in strains that are resistant to antibiotics, current staple treatments are becoming less effective with time, necessitating the requirement for alternate medicines. Acne has been successfully treated using phototherapy, and there is currently a resurgence of interest in photodynamic therapy as a method of care. The key benefits of PDT over other therapy techniques are its high remission rates despite being minimally invasive and outstanding cosmetic results.

A high level of cosmesis is required in the therapy choice for basal cell carcinoma BCCs because of their propensity for developing in the head and neck. Typically, surgical excision is the preferred treatment for nodular BCCs. Exophytic components of the lesions should be first

removed for BCCs that are thicker than 2-3 mm [22]. BCCs have been successfully treated with PDT and carbon dioxide (CO<sub>2</sub>) laser when used as monotherapy, with the superficial histologic subtype seeing the best results. When used alone, these treatments have a number of drawbacks when compared to surgical excision, including as PDT's limited depth of penetration (2 mm absorption), which may reduce its effectiveness in treating nodular BCCs with thicknesses higher than or equal to or greater than this.

**Skin-related T-cell lymphoma** The most prevalent primary cutaneous T-cell lymphoma is mycosis fungoides (MF) (CTCL). Unilesional MF is distinguished by a chronic yet indolent course and a restricted skin involvement.

Treatments include targeted chemotherapy, photochemotherapy, and radiotherapy are options if lesions are resistant to topical steroids. They do, however, have a number of acute and long-term negative effects, and toxins may build up if prolonged and repeated treatment cycles are given to lesions that are refractory or recurrent. [20-22] For nonmelanoma epithelial skin malignancies, photodynamic therapy is an effective treatment after topical 5-aminolevulinic acid administration.

Additionally, it has been used successfully in cases of cutaneous T-cell lymphoma. More recently, a silicon phthalocyanine Pc 4-PDT clinical trial has been started at Case Western Reserve University (CWRU, Cleveland, USA). The benefits of Pc 4 have been demonstrated to include strong absorption at longer wavelengths, relative photostability, and, when applied topically, a shorter drug-light interval. T-cells were discovered to be more vulnerable to Pc 4-PDT-induced apoptosis than keratinocytes in preclinical experiments [23].

In a recent study, 30 patients with mostly thin-grade AK of the face or scalp were treated with 16% and 8% MAL-PDT in two symmetrical areas after applying sunscreen. The study compared response rates and side effects after PDT using conventional 16% and 8% MAL with home-based daylight exposure for the treatment of AK. The patients were told to spend the rest of the day outside at home in daylight before leaving the hospital.

During treatment, patients recorded their level of pain, and a wristwatch dosimeter device was used to measure their exposure to light. After three months, the total response rate for 16% MAL was 76.9%, and for 8% MAL, it was 79.5% ( $P=0.37$ ). Similar reaction rates were produced by light intensities of 8–70 J/cm<sup>2</sup> ( $P=0.25$ ).

Patients felt mild to moderate pain when exposed to sunlight (a mean maximal pain score of 3.7). There were no differences between the areas treated with 16% MAL and those treated with 8% MAL in terms of pain ratings or erythema [24].

### Future

PDT is based on a straightforward premise, but because it involves so many variables, it is complicated. More research is needed to identify the precise variables that are best for treating each condition. [24-26] This would include aspects of the photosensitizing chemicals, like route of delivery and time spent applying them, as well as aspects of the light, like its wavelength, duration, and intensity.

PDT has also been successfully used for a variety of off-label uses. It would be easier to get their FDA clearance if there was more information and evidence on the effectiveness and safety of PDT in treating conditions including actinic cheilitis, psoriasis, and acne vulgaris.

The same would apply to PDT in aesthetic dermatology, where it is gaining momentum and requires careful investigation for widespread and secure application.

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