Clinical Potential of Photodynamic Therapy in Skin Disorder

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LETTER TO EDITOR

Dear Editor,

Skin cancer patients may benefit from photodynamic therapy (PDT), which employs light exposure to activating medicine that produces cytotoxic damage solely to the diseased skin. Photodynamic therapy (PDT) is increasingly popular in dermatology due to its discovery in the early 20th century and the advent of topical photosensitizers. A second-generation photosensitizer, such as 5-aminolevulinic acid and methyl aminolaevulinic acid, are now being developed for the treatment of actinic keratoses. As an alternative to more invasive therapies, PDT's non-invasive nature and portability make it an attractive option. Shorter recovery durations and better-looking cosmetic results are also associated with this method. PDT has been proven to be useful in the treatment of various non-melanoma skin cancers because of these benefits. In addition to skin cancer, photodynamic treatment may help to treat cutaneous T-cell lymphoma, psoriasis, acne, and leishmaniasis. Photosensitizers are light-activated chemicals that may be used to kill certain cells. The Nobel prize-winning scientist Hermann von Tappeiner and his student Oscar Raab discovered that acridine orange is toxic to paramecia protozoa when exposed to light. When Von Tappeiner and dermatologist Jan Jesionek used cosin and light in 1903, it was the first clinical application of PDT on humans. When they described this phenomenon in their textbook as an oxygen-dependent process, they created the term "photodynamic reaction" [1, 2]. Reactive oxygen species (ROS), mostly singlet oxygen, are formed when a photosensitive substance is triggered by light. Several studies have shown that reactive oxygen species (ROS) cause oxidative damage to biological components, necrosis, autophagy, and cell death. When cells die, they go through a process known as apoptosis. In 1991, Agarwal, et al., discovered apoptosis as a response to PDT for the first time. Sensitizers present in mitochondria, such as 5-aminolevulinic acid (ALA), may promote PDT-induced apoptosis. Besides cell death, PDT causes vascular damage and activates inflammatory mediators indirectly, which contributes to its effectiveness [3, 4].

The most prevalent photosensitizer in PDT is hematoporphyrin, an endogenous porphyrin first synthesized from heme in the mid-19th century. Photodynamic effects of hematoporphyrin on paramecia and skin of mice exposed to light after systemic therapy were described by Hausmann in 1911 [5]. Policard in France discovered hematoporphyrin in cancerous tissue in 1924, and German researchers Auler and Banzer did the same thing in 1942 [6, 7]. Hematoporphyrin was replaced with a pure hematoporphyrin derivative (HpD) found by Schwartz in the mid-20th century because of its significant phototoxicity [8]. Photofrin® (Axcan Pharma, Birmingham, AL), a purer HpD porphyrin sodium, was the first systemic photosensitizer to be approved by the FDA. The long-lasting and extreme photosensitivity associated with systemic photosensitizing medications remained a major drawback even though HpD was more effective in detecting tumors and required lower doses than crude hematoporphyrin. Actinic keratoses (AK) is the most common precancerous skin lesion. As a consequence of frequent exposure to UV radiation, a condition known as "field cancerization" might arise. A single lesion's yearly transformation rate ranges from 0.025% to 16%. "Squamous cell carcinoma (SCC) was shown to account for 60% of the development of AK in a longitudinal study by Marks, et al.," Contiguous AKs were shown to be responsible for 97% of all SCC cases in another investigation [9]. These lesions seem to be harmless, but the physician must decide whether or not to treat them, since there is no reliable method to predict which patients may benefit from treatment. Traditional treatments for actinic keratoses (AKs) include cryosurgery, 5-fluorouracil, and curettage, all of which have side effects. It is possible to treat the nonhyperkeratotic face and scalp AKs well with MAL or ALA-PDT, with cure rates of up to 100%. The FDA approved the first topical PDT agent, ALA, for this application in December 1999.

In 2001, Jeffes, et al., showed that ALA-PDT was successful in the treatment of multiple AKs in a blinded clinical trial [10]. Only 6% of the AKs in the placebo-PDT group reacted fully to ALA application followed by blue light irradiation, while 85% of those reacted on the face and scalp. In a multicenter study, ALA-PDT was shown to be both safe and effective in the treatment of AKs, eliminating up to 75% of the AKs in 89% of individuals after 12 weeks.

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It has been shown that the clearance rates of conventional treatments are comparable. A study conducted by Kurwa, et al., in Europe, found no statistically significant difference between patients treated with ALA-PDT once and those treated with 5-fluorouracil three times a week in the reduction of the lesioned area [11]. Smith, et al., discovered that ALA-PDT was more tolerable and aesthetically attractive than 5-fluorouracil in the treatment of AK. More recent studies have looked at the long-term impact of ALA-PDT on AKs [12]. After re-examining patients 12 months after the treatment with ALA-PDT, researchers from numerous centres observed that a percentage of previously cleared lesions had recurred. For this, Tschen, et al., surveyed 12-month follow-up research on their patients. On the histology, 7% of the recurrent lesions had SCC. Because PDT did not affect the rate of SCC, it may be concluded that it is not carcinogenic [13].

According to the clinical trial data, there is strong evidence to support the use of ALA and MAL to treat AK.

MAL has been licensed by the FDA since 2004 for the treatment of AK and basal cell carcinoma, while it has been authorized in Europe since 2001. According to Pariser, et al., 86% - 89% of AK lesions demonstrated complete lesioned response after two MAL-PDT treatments with red light [14]. In the study of Tarstedt, et al., a single MAL-PDT therapy was as effective as two treatments in achieving complete responses [15]. Although the two-treatment schedule was better for thicker lesions (93%), it was also more effective overall (89%) and Acute Kidney Failure (AKF) responds to MAL-PDT at least with the same effectiveness as cryotherapy, according to these results. MAL-PDT and cryotherapy were compared in a study by Szeimies, et al., which indicated that both therapies had identical response rates at 3-month follow-ups (67% versus 75%) [16]. In research by Freeman, et al., two sessions of MAL-PDT provided significantly higher efficacy than cryotherapy in the treatment of AKs (91% versus 68%) [17]. It is possible that in the future MAL will be more successful in boosting lesion concentrations than ALA since it penetrates AK more effectively than ALA does. The efficiency of MAL-PDT and ALA-PDT was shown to be the same in a small, double-blind, randomized prospective study conducted by Lai, et al. [18].

AKs are particularly susceptible to PDT when applied to the skin using topical ALA or MAL. If you have several AKs, you may want to consider PDT since it may cure many lesions at once. Patients having AKs in cosmically sensitive areas, such as the face, have exhibited a better aesthetic result than that of cryotherapy, and symptoms of photoaging have been relieved. For AK, PDT is safe and very successful, leading to happier patients, quicker healing periods, and improved cosmetic results.

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REFERENCES


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