A new PDT technique in Actinic Keratosis Treatment and in NMSC (Non Melanoma Skin Cancer) prevention

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ACTINIC KERATOSIS

It is one of the most frequent secondary cutaneous diseases caused by sun rays exposure. Scientific evidences showed it is a real squamous in situ cell carcinoma. Squamous cell carcinoma is one of the most aggressive cutaneous cancers, with metastasis risk estimated between 0,5% and 33%.
CLINIC ACTINIC KERATOSIS

It is an indefinite round shape macula, variable in colour from reddish to yellowish brown, surmounted by continuous desquamation, rough to the touch, with variable dimension from a few mm to several cm. It can present itself in a single or multiple shape (cancerization field) and primarily affects the sun-exposed areas, mainly face and scalp. According to the Skin Cancer Foundation it affects 50% of people over 50 years.

Risk factors include: light phototype, male gender, latitude, extended exposure to sunlight (particularly UVB), and genetic factors. Also, immunosuppressive therapies, cancer, inflammatory diseases, use of tanning beds.
Classification according to clinical features:

- Group I: barely visible and barely palpable lesion
- Group II: barely visible but palpable lesion
- Group III: frankly visible and hyperkeratotic lesion.

The risk of neoplastic transformation is estimated between 0.1% and 20%
It looks like a very superficial in situ squamous cell carcinoma, just on the epidermis level, characterized by the presence of atypical keratinocytes, with large and pleomorphic nucleus, eosinophilic and vacuolated cytoplasm, altered nucleus / cytoplasm ratio and alteration of the polarity of keratinocytes that can no longer have an organized maturation. The histopathological variants currently described are: hypertrophic, atrophic, bowenoide, acantholytic, lichenoid and pigmented.
THERAPY

Therapies offered to date are many and range from surgical excision, to cryotherapy with liquid nitrogen, from electrosurgical ablation laser, to topical therapies such as 5-fluorouracil. Currently, imiquimod at 5% and diclofenac at 3%, up to the most recent ingenol mebutate, are the most used medications. Since some years photodynamic therapy (PDT), is also used.
PDT

Cutaneous Photodynamic therapy (PDT) is a non-invasive method that uses a topical photosensitizing substance combined with a luminous source, in order to induce the selective destruction of cancer or altered cells.

The technique is based on a photodynamic reaction, chemical process mediated by the light, which is absorbed by a photosensitizing substance and subsequent formation of oxygen reactive species (ROS) which, interacting with the altered cutaneous cells, determines its death by apoptosis or necrosis through photophysical, photochemical and photobiological mechanisms. The substances used as photosensitizers are intermediate products of protoporphyrin IX synthesis, such as methyl-aminolevulinate and the 5-aminolevulinic acid (5-ALA), which are small molecules, non-toxic to humans. The Light represents the necessary energy to activate the drug; for this purpose many luminous sources can be used, providing that the emission is stable and the irradiation field is homogeneous.
PDT WITH LED

In the phototherapy field the use of LED luminous sources is spreading. These luminous sources (Light Emitting Diode) emit low doses of energy, in intermittent or continuous mode. Similarly to LASER, LEDs are able to emit a monochromatic light beam but without mono-directionality. The power generated by LED is in the order of mWatt, while the LASER power ranges from mWatt to megaWatt.

The action mechanism of LED systems is not yet fully known. The interaction between electromagnetic radiation of low intensity and cellular structures, the system of Cytochromes, placed at the level of the mitochondrial membrane, would be the most important receptor system in luminous stimulus conversion. It has been demonstrated an action on fibroblasts and other cell lines. The collagen synthesis by fibroblasts and their proliferation has been demonstrated with several LED systems at different wavelengths.
PDT LED

In recent years several clinical studies have showed promising results on wound healing disorders, inflammations and photoaging damages. A study shows the preventive effect of LED radiation on an induced dermatitis, by ionizing radiation in patients with breast cancer. Finally, recent clinical studies place the focus on the use of LED systems in acne treatment especially in the inflammatory phase.

Led equipment are generally constituted by panels on which a number of individual Leds are fitted. The patient is positioned at a distance of a few centimeters (5-10) from the radiating panel. Different wavelengths are used, the most versatile is the red one which has an excellent penetration through the epidermis and dermis layers. Most Led systems provide a continuous emission, but recent studies also demonstrate the effectiveness of instruments that offer a pulsed emission, in particular in the yellow, red and infrared wavelengths, with faster application times.
The new LED device EPIC with YOUNG AGAIN® technology, used at our Clinic, as opposed to any other method, presents a series of LED diodes placed inside an anatomical mask which is applied at an average distance of about 5-10 mm from the skin. This innovative technique was born from the need to make the field the most uniform reducing also the time of exposure to light.

This method is indicated for the treatment of multiple cases ranging from multiple Actinic Keratoses to photoaging and, for its safety and effectiveness, can be applied to all patients. Thanks to various ALA concentrations (from 5% to 20%), its use is modulated for different pathologies and 10-15 minutes of irradiation are enough to obtain the first results.

Working at a minimal distance (5-10 mm), tissues receive all the energy emitted without any dispersion.
The device we use, Epic with YOUNG AGAIN® technology, is the only one to provide a radiation at about 10 mm from the skin. This characteristic makes it particularly effective because it avoids any loss of energy and allows to work at relatively low powers, thus decreasing pain and improving patient compliance.
In our Oncological Dermatology Service at “Marco Polo” Hospital we selected 15 patients, 10 males and 5 females, ages between 54 and 77 years, with multiple face Actinic Keratoses. We used 5-ALA in cream at 10% with occlusive bandage for an average duration of about two hours. Subsequently we irradiated with light at 633nm LED for 15-20 minutes with pulsed mode. For each patient, we performed three treatments at a distance of one month.
We saw the patients on the seventh day and made further checks at one and three Months. The results have shown the complete disappearance of the Actinic Keratoses together with a considerable improvement in skin texture. LED irradiation at such minimal distances (5-10mm) is able to stimulate the skin, producing visible effects also on surrounding skin surface. At follow-up checks, skin is more luminous and tighter and patients described well-being sensations.

We believe that this may have a positive role in the so-called cancerization field (the skin surrounding the lesion may become the site of genetic alterations and of initial and gradual replacement of normal cells with anomalous ones), therefore the formation of precancerous lesions and subsequent NMSC.
The **YOUNG AGAIN®** technology could become a valid tool in the treatment of precancerous lesions and to prevent the onset of NMSC. Finally, in addition to the well known advantages of PDT, such as lack of invasiveness and systemic toxicity, selectivity and negligible side effects, we remember that the new technology with 633nm mask is currently the only patented PDT where the distance between the skin and the LED does not exceed 10 mm; this optimizes the absorption by the altered cells, reducing the time of exposure and favoring patient compliance.
A case report

PDT with 5-ALA at 10% in occlusion for 2 hours and subsequent irradiation with YOUNG AGAIN® technology. A 79 year-old patient had numerous actinic keratoses on the face, treated several times over the years with other techniques (cryotherapy with liquid nitrogen).

The patient received 3 treatments, one per month.

Picture A at T0.

Picture B exfoliation at 10 days after each treatment.

Picture C at 15 days from last (3d) treatment.
Bibliography


L’utilizzo Del Piroxicam Gel 1% Nel Trattamento Delle Neoplasie Epiteliali cutaneeEUR ediz 2010 Di Francesca Specchio