

## Photodynamic Therapy with 5-Aminolevulinic Acid (ALA) in the Treatment of Acne: A Case Study

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### ABSTRACT

Photodynamic Therapy (PDT) is characterized by a combination of a photosensitizing compound that is retained in the tissues, followed by illumination with light, which causes a photoreaction. Its action occurs mainly through mechanisms of energy transfer between the excited Photosensitizer (PS) and the molecular oxygen present in the tissues generating reactive oxygen species, with possible reactions with the tissue. Topical PDT with 5-aminolevulinic acid (ALA) and its derivative as methyl aminolevulinate (MAL), which are precursors of the formation of Protoporphyrin IX (PpIX), has been occupying a growing space in aesthetic dermatology in special for facial rejuvenation, in the treatment of melasma, scars, stretch marks and acne. In this sense, due to the potential of PDT for the treatment of local infection and the stimulus to the process of tissue remodeling, the interest in studying the possible aesthetic applications of PDT in the acne treatment is relevant. Therefore, this case study aimed to evaluate the effects of PDT in the treatment of acne using an ALA cream at 2%, and light source designed specifically for this purpose. The case report aims indicate this procedure to severe cases of acne.

### Introduction

Acne is a chronic inflammatory disease of the pilosebaceous unit. Its etiology is related to the alteration in the process of keratinization of the epidermis that hinders the drainage of the secretion produced by the sebaceous glands [1-3]. Many factors are involved in the physiology of acne such as sebaceous hyperproduction, follicular hyperkeratinization, periglandular dermal inflammation and increased bacterial colonization by *Propionibacterium* acnes. The presence of inflammation and infection lead to the formation of different types of scars on the skin [1,4,5]. It is considered a common dermatological problem among young people, with no easy solution.

Dermatological treatments consist of topical and oral administration of antibiotics (topical and systemic), isotretinoin, anti-inflammatory, hormonal therapy and surgical treatment (removal of pustules and scars) [6,7]. The most usual treatments in dermatological clinic therapy are with antibiotics. However, the exacerbated administration is able to generate resistance (~ 40- ~ 60%) which reduces its efficacy. In addition, the combined use of systemic and

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topical antibiotics can lead to the death of most of the bacteria present on the skin, which results in a negative effect on the skin homeostasis [5,8].

Photodynamic Therapy (PDT) has been widely used in the treatment of skin cancer through the interaction of light with an exogenous photoreceptor, or in the case of ALA, an endogenously produced porphyrin. This photosensitive substance has the ability to absorb light with subsequent energy transfer to the tissue in the form of oxygen generating a high amount of singlet oxygen. In turn, these will produce a fraction of necrosis or apoptosis with a local inflammatory response for stimulating tissue regeneration [9-14]. The equivalent process, also promote microorganism elimination with infection-free healing.

In this sense, due to the potential of PDT for the treatment of local infection [15] and the stimulus to the process of tissue remodeling, the interest in studying the possible aesthetic applications of PDT increased [9-14]. Therefore, this case study aimed to evaluate the effects of PDT in the treatment of acne, such as reducing the level of acne severity and demonstrated better quality of the regenerated tissue. Reported cases are important to transmit experience to professionals, promoting access to information.

### Case presentation

This study was carried on with a female volunteer, 24 years old, skin photo type I, with severe acne, characterized by the presence of pustules, nodules, and cysts painful and inflamed areas (Figure 1A). The patient report years of problems with many tries with conventional therapy without satisfactory results. A single PDT session was performed using a prototype of illumination device developed in cooperation with MM Optics Company at the São Carlos Institute of Physics (Laboratory of Technology Support, São Carlos, SP, Brazil). This prototype consists of 30 LEDs emitting in the region of the red spectrum (630 nm), and 25 LEDs emitting in the region of the blue spectrum (450 nm) 20. The operator can make can choose the appropriate color for each case. For this case, the treatment was performed using red spectrum (630 nm), due to the

necessity for deeper penetration. Figure 1 presents the illumination device.

The photosensitization of the areas was done with 5-Aminolevulinic acid with the concentration of 2% (2%-ALA) provided by PDT PHARMA® (Cravinhos, SP, Brazil) mixed with a nonionic base cream (pH 3 - 3.5), following the manufacturer's recommendations.

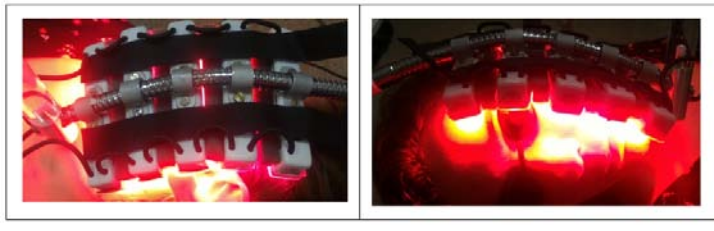
For first comparison and demonstration, only the left side of the patient's face received the treatment, which was previously sanitized with a solution of chlorhexidine. At this point, the first photo was taken. After this, the base cream blend with 2%-ALA was evenly applied in the acne lesions, forming a thin layer of about 0.5 mm average thickness. The area that received the cream was occluded with plastic film and aluminum foil to protect from room light. After 3 h of incubation, the area was cleaned with wet cotton gauze to remove the excess ALA. The lesions were exposed to light using the illumination device. The LED emitters were positioned perpendicular to the skin. The parameters used in the treatment were: wavelength 630 nm (red). The irradiance of 40 mW /cm<sup>2</sup>, the dose of 25J /cm<sup>2</sup>, obtained with an illumination time of about 10 minutes.

After the treatment, the volunteer was instructed to routinely use moisturizing cream and sunscreen (home care). To observe the evolution of the treatment photographic evaluations were performed 1, 3, 7 days after treatment. After the final observation, the second face was treated with the equivalent procedure.

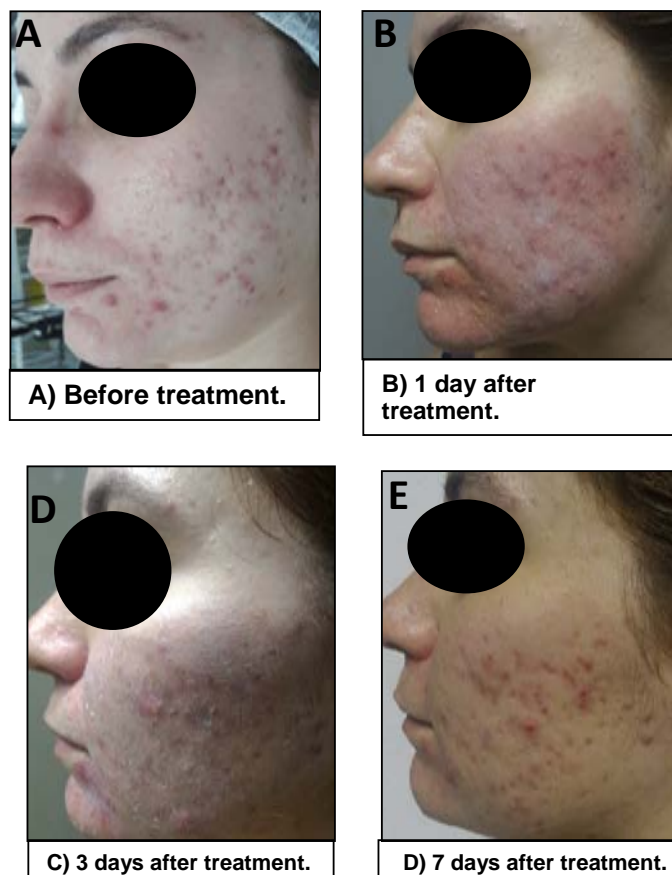
### Discussions

Cosmetic photodynamic therapy is an area with the great potentiality to help in cases of acne severe. Although the technique is widely used in actinic keratosis, it is well controlled to be applied in cases of non-pre-malignant lesions as well. Many authors [7,9,16-21] have proven the technique to be highly effective.

It is, like in this presented case, an excellent alternative for patients who fail conventional type of treatments as well as for those that react to conventionally used topical or systemic medication. In special, the recent request to attenuation of the use of antibiotic due to bacterial resistance, PDT gets in the picture as a more attractive possibility.



**Figure 1:** Illumination device for large area application, operating with intensity up to 40 mW/cm<sup>2</sup> of either 630 nm or 450 nm.



**Figure 2:** Aspects of the treatment evolution. (A) Before treatment. (B) 1 day after treatment. (C) 3 day after treatment. (D) 7 day after treatment.

The mechanism of action of PDT is not yet fully established even though, the general aspects are quite well understood. It seems that factors like the technique promote the *Propionibacterium acnes* level decrease with changes in the sebum excretion followed by immune system modulation are potential contributions. The inhibition of sebum secretion by injuring the tissue certainly contributes. Another important factor is the sterilization of the follicles with subsequent reduction of follicular obstruction.

Considering that PDT with ALA has several side effects, such as edema, high hyperemia (reddish skin), high photosensitization, high local inflammation and even post inflammatory hyperpigmentation. These effects are dependent on ALA concentration, incubation time and irradiation dose [13,17,21]. Thus, in aesthetic applications, low irradiance (mW) and low and medium light doses (J/cm<sup>2</sup>) were used to minimize these effects [9-14,18]. The results showed very well controlled side effects.

Despite this, the effects of skin hypersensitivity were reported immediately after treatment by voluntary and the complaint lasting up to two days after the PDT session. In addition, we can observe local hyperemia in figures 2B and 2C, being more exacerbated in Figure 2B compared to 2C.

As previously described, the volunteer had inflamed pustules and cysts (Figure 2A). After PDT we observed a gradual reduction on days 1 and 3 (Figures 2B and 2C), with a considerable reduction on the seventh day after PDT (Figure 2D).

Our results are in accordance with the literature that describes that after an injury, hemostasis occurs as the initial stage and basis for the healing process, followed by inflammation resulting in vasodilation and increased vascular permeability. This process is classically described with a duration of 4 to 6 days [19].

Those effects, are however fully controlled with the correct classification for the patient.

### Conclusion

The results obtained in the present study suggest that PDT with 2%-ALA was effective in the treatment of severe acne, reducing the severity of acne. However, new studies need to be done in order to find a protocol that minimizes the side effects of PDT and guarantees the beneficial effects. Reporting cases like this are quite important for the construction of experience that may transfer the procedure into more standard acne.

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