

# Overcoming a Too Painful Conventional Methyl Amino-Levulinic Photo Dynamic Therapy (MAL-cPDT) Session for Scalp Actinic Keratosis with Topical Anesthesia: A “N Of 1” Trial Case Report

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## Abstract

Conventional Photodynamic Therapy (cPDT) with Methyl Amino-Levulinic (MAL) is considered a very effective treatment of Actinic Keratosis (AK) lesions. However, its use is limited by the fact that this procedure could be very painful. Topical anesthesia could be effective in reducing pain during cPDT. A recent controlled randomized trial has shown that the use of the preventive application of the self-occlusive lidocaine 7%-tetracaine 7% peeling off cream is very effective in reducing the procedure-associated pain during MAL-cPDT for the treatment of AK lesions. However, this is not so far, a routine method for PDT procedures. In particular there are no data regarding the efficacy of this approach in subjects with a history of too painful early interrupted cPDT sessions. Here, we report a clinical case of a subjects with multiple scalp AK lesions with a history of unsuccessful cPDT session early interrupted ( $\leq 2$  minutes) because heavy pain (100 on a 0-100 mm Visual Analogue Scale). Two weeks later, we decided to perform a MAL-cPDT session with the use of self-occlusive topical anesthesia (lidocaine 7%-tetracaine 7% peeling off cream) applied for 1-hour. Occlusive MAL application for 3 hours was then done followed by cPDT with a fluence of 32 J/cm<sup>2</sup>. The session was quite well tolerated (VAS score 50), allowing to complete the programmed 8-minute session. At the follow up, a complete clearance of AK lesion was documented. This “N of 1 study” case report demonstrated that topical anesthesia with lidocaine/tetracaine 7% auto-occlusive peeling-off cream applied before cPDT is an effective strategy in subjects with an history of pain-related incomplete cPDT session.

**Keywords:** Conventional PDT; Lidocaine; N of 1 trial; Tetracaine; Topical anesthesia

## Introduction

Conventional Photodynamic Therapy (cPDT) is considered a very effective treatment of Actinic Keratosis (AK) lesions, mainly when they are located on the scalp and face [1]. However, its use is limited by the fact that this procedure could be very painful [2]. In some case the level of pain perceived by the subject could cause the premature conclusion of the irradiation session [3]. Topical anesthesia could be effective in reducing pain during cPDT. A recent controlled randomized trial has shown that the use of the preventive application of the self-occlusive lidocaine 7%-tetracaine 7% cream is very effective in reducing the procedure-associated pain during methyl Amino-Levulinic (MAL)-cPDT for the treatment of AK lesions [4]. Several clinical trials have demonstrated that this cream can reduce dermatological procedure associated pain by -41% in comparison with vehicle, with an effective anesthetic effect up to 9 hours [5]. This latter aspect could be particularly relevant taking in account that in cPDT the photosensitizer (i.e. methyl amino-levulinic acid) should

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be applied for 2-3 hours before the irradiation session, therefore if an anesthesia strategy should adopted in this clinical setting this time-lag period should be taken in consideration. Topical anesthesia with this cream however is not so far, a routine method for PDT procedures. In particular there are no data regarding the efficacy of this approach in subjects with a positive history of too painful early interrupted cPDT.

## Case Report

Here we report an “N of 1” study-like case report. A man, 82 years old, Fitzpatrick phototype 2, with a 10-years history of multiple ( $\geq 15$  lesions) AK lesions located on the scalp, face and on the dorsal hand went to our attention on August 20, 2021. Previous treatments were topical diclofenac and then ingenol mebutate. Clinically significant recurrence of lesions was observed after each topical treatment. We decide to perform a MAL cPDT session for the treatment of scalp lesions using a Red light source lamp (standard fluence 37J/cm<sup>2</sup>) (LED Red light 630 nm; Aktilite lamp; Photocure ASA, Oslo, Norway). MAL 16% (Metvix, Galderma) was applied according to manufacture’ use indications with 3 hours application time with occlusive dressing. After 2 minutes the cPDT session should be interrupted because the appearance heavy pain (100 on a 0-100 mm Visual Analogue Scale). Two weeks later, we decided to perform a cPDT session with the use of self-occlusive topical anesthesia (lidocaine 7% and tetracaine 7%) applied for 1-hour (Figure 1). After 1 hour the product could be removed easily (self-occlusive peeling off cream). Occlusive MAL application for 3 hours (Figure 2) was then done followed by cPDT session with the same modalities of the previous one. The session was quite well tolerated (VAS score 50), allowing to complete the programmed 8-minute session. At the follow up, a complete clearance of scalp AK lesions was documented.



**Figure 1:** Application of self-occlusive lidocaine 7%-tetracaine 7% cream in the scalp area for 1 hour before MAL application.



**Figure 2:** MAL 3-hour application with occlusive dressing just before cPDT session.

## Discussion

Conventional PDT is a very effective treatment of AK and others skin cancers at the early stage [6]. Conventional PDT is considered the standard treatment procedure to control field cancerization [7]. The pain associated with cPDT could limit the general use of this procedure. In some cases, the pain could cause the early termination of treatment session with a consequent decrease of the overall therapeutic efficacy. A recent controlled randomized trial has shown that the use of the preventive application of the self-occlusive lidocaine 7%-tetracaine 7% peeling-off cream is very effective in reducing the procedure-associated pain during cPDT for the treatment of AK lesions in “naïve” subjects. There are no data regarding the efficacy of this approach in subjects with a positive history of too painful early interrupted cPDT.

## Study Limitations

Some limitations should be taken in account in assessing the present work. First of all, it is a single case report. However, the present

case report could be considered a kind of “N of 1 trial” [8]. An N of 1 trial is a clinical trial in which a single patient is the entire trial, a single case study. This type of study has enabled researches to obtain experimental progress without the massive work of designing a group comparison study. The N of 1 trial could be very effective in confirming causality. A second study limitation is related with the fact that algesia level during a cPDT could vary between sessions. Therefore, the different pain score we have registered in the present case could be in part influenced by this aspect.

## Conclusion

This “N of 1 study” case report demonstrated that topical anesthesia with lidocaine/tetracaine 7% auto-occlusive peeling-off cream applied before cPDT is an effective strategy in subjects with an history of pain-related premature stopped cPDT session.

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