

# Pain, pain relief and other practical issues in photodynamic therapy

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We have been using photodynamic therapy (PDT) at the Department of Dermatology, Sahlgrenska University Hospital in Göteborg since the 1990s, so we have gained considerable experience with the technique.

Sometimes patients experience pain with PDT. Such pain typically involves a burning, stinging and prickling sensation during illumination, which arises quickly (within a few seconds to a minute after commencing illumination), peaks quickly and then levels off. In some patients pain persists for a longer duration (up to 24 h), and there have been a few rare cases where pain has lasted for several days after treatment. The mechanism of this pain has not been fully elucidated; with aminolevulinic acid (ALA) PDT, the gamma amino butyric acid (GABA) receptor system may be involved, because ALA is transported into peripheral nerve endings by GABA receptors. This can result in fibre stimulation and pain. Other mechanisms may also be involved.

Pain is influenced by different parameters. For example, increasing temperature results in more pain, and there have been some reports that shorter light wavelengths (e.g. green or blue) cause less pain. It has been shown that ALA PDT causes less pain than cryotherapy, and a similar level of pain to 5-fluorouracil.

In another study using cold-air anaesthesia in 26 patients each with two basal cell carcinomas (BCC), ALA PDT was performed on one BCC without concurrent cold air administration, and the other with cold air. Less pain occurred in those treated lesions receiving cold air.<sup>5</sup>

In our study of ALA PDT with EMLA, we noted considerable interpatient variation in the pain experience, with 5–10% of patients experiencing quite severe pain, mainly with extensive actinic keratoses, and about the same percentage experiencing no pain at all. The remainder had an intermediate level of pain that could be managed with cool fans and cool water.<sup>2</sup>

Assessment of the pain levels associated with treatment of different lesions types found that solar keratoses (SK) resulted in most pain, and BCC the least. Lesions on the head caused more pain than those on the trunk and extremities. On the head itself, more pain occurred on the scalp and forehead, and larger areas caused more pain than smaller areas. No differences in pain were observed for different skin types.<sup>2</sup>

Similar results were obtained in a study of 100 SK patients, although there was a tendency for patients with skin type IV to have less pain. (Sandberg C, personal communication). In a study of 37 patients with SK we found no significant differences in pain during PDT, when the fluence rate was varied between 30 and 70 milliwatts/cm<sup>2</sup>. The pain was most intense up to a light dose of 20 J/cm<sup>2</sup>.<sup>4</sup>

## MANAGING PAIN IN PHOTODYNAMIC THERAPY

The first approach to managing pain in PDT should be to discuss the possibility of its occurrence with the patient before commencing treatment.

Pre-treatment pain reduction strategies include use of a benzodiazepine, topical anaesthetic, nerve block, epidural or even general anaesthesia. During treatment we have found the most effective approach is to use cooling fans or water sprays on to the treatment site. Also, the light intensity may be lowered (thus prolonging the treatment) and short breaks may be taken during illumination without loss of efficacy.

There has been some interest in the use of topical anaesthesia. No significant reduction in pain was found during ALA PDT when using a tetracaine gel,<sup>1</sup> and our assessments have found that topical eutectic mixture of local anaesthetics (lidocaine and prilocaine) (EMLA) is similarly ineffective with ALA PDT.<sup>2</sup> When patients are in pain we infiltrate with local anaesthetic, using either 0.5% lidocaine and adrenaline, which provides relief for approximately 1.5 h, or bupivacaine with adrenaline, which has a longer duration of effect (2–6 h).

## PAIN WITH METHYL AMINOLEVULINATE PDT VERSUS AMINOLEVULINIC ACID PDT

Is there a difference in pain between ALA PDT and MAL (Metvix) PDT? In a double-blind randomised study in tape-stripped normal forearm skin, MAL PDT was shown to be significantly less painful than ALA PDT.<sup>5</sup>

## THE FUTURE

In the future, pain management options may include *trans*-nervous stimulation, biofeedback systems, acupuncture, lowering the fluence rate, or using an intermittent dosage.

## REFERENCES

1. Holmes MV, Dawe RS, Ferguson J, Ibbotson SH. A randomized, double-blind, placebo-controlled study of the efficacy of tetracaine gel (Ametop) for pain relief during topical photodynamic therapy. *Br. J. Dermatol.* 2004; 150: 337–40.

2. Grapengiesser S, Ericson M, Gudmundsson F, Larko O, Rosen A, Wennberg AM. Pain caused by photodynamic therapy of skin cancer. *Clin. Exp Dermatol.* 2002; **27**: 495-7.
3. Pagliaro J, Elliott T, Bulsara M, King C, Vinciullo C. Cold air analgesia in photodynamic therapy of basal cell carcinomas and Bowen's disease: an effective addition to treatment: a pilot study. *Dermatologic Surg.* 2004; **30**: 65-6.
4. Ericson M, Sandberg C, Stenquist B *et al.* Photodynamic therapy of actinic keratosis at varying fluence rates: assessment of photobleaching, pain and primary clinical outcome. *Br. J Dermatol.* 2004; in press. 3
5. Wiegell SR, Stender IM, Na R, Wulf HC. Pain associated with photodynamic therapy using 5-aminolevulinic acid or 5-aminolevulinic acid methylester on tape-stripped normal skin. *Arch. Dermatol.* 2003; **139**: 1175-7.

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