

Photodynamic therapy for treatment of Acne Vulgaris in clinical studies; dose response and mode of action

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Avhandlingen baseras på följande delarbeten:

- I **C. Hörfelt, J. Funk, M. Frohm-Nilsson, D. Wiegleb Edström and A-M. Wennberg.** Topical methyl aminolaevulinate photodynamic therapy for treatment of facial acne vulgaris: results of randomized, controlled study
Br J Dermatol 2006; 155: 608-13
- II **C. Hörfelt, B. Stenquist, O. Larkö, J. Faergemann and A-M. Wennberg.** Photodynamic Therapy for Acne Vulgaris: a Pilot Study of the Dose-Response and Mechanism of Action
Acta Derm Venereol 2007; 87: 325-329
- III **C. Hörfelt, B. Stenquist, C.B. Halldin, M.B. Ericson, A-M. Wennberg**
Single low dose red light is as efficacious as MAL-PDT for treatment of acne: Clinical assessment and fluorescence monitoring
Submitted for publication.
- IV **C. Hörfelt, N. Karami, J. Faergemann, A-M. Wennberg, M.B. Ericson,**
Photodynamic effect in Propionibacterium acnes: An in vitro study investigating the effect of red and blue light in the presence and absence of aminolevulinic acid or its methyl ester
Submitted for publication.

Photodynamic therapy for treatment of Acne Vulgaris in clinical studies: dose response and mode of action

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Abstract

This thesis deals with the use of photodynamic therapy (PDT) for treatment of Acne Vulgaris. Acne Vulgaris is one of the most common skin disorders. Conventional treatments target the pathogenic factors and include a variety of topical and oral medications such as antibiotics. Many patients show no clinical response or experience side effects from these conventional therapies. The wide use of antibiotics leads to bacterial resistance, and hence there is a need for new alternatives in acne treatment. Photodynamic therapy (PDT) is based on an initial photosensitization of the skin, followed by irradiation with visible light producing cytotoxic singlet oxygen. When PDT is applied for treatment of acne it is believed to affect the sebaceous gland and the bacterium *P.acnes*; however, the full mechanism involved in PDT of acne is not clear. The work in this thesis deals with investigating mechanisms of action and the most effective treatment regimen for PDT of acne.

Patients with mild to severe acne have been studied. In a nonblinded dose finding study, patients received aminolaevulinic acid (ALA) PDT at different light doses on the cheeks and on the back. No significant difference in clinical result was found between the different light doses of ALA-PDT, although pain and hyperpigmentation were more common at higher doses. In a split-face placebo-controlled blinded study, patients received two consecutive methylaminolaevulinate (MAL) PDT and placebo treatment. Greater reduction in total inflammatory lesion count was obtained with two consecutive MAL PDTs compared with placebo PDT; however, in another split-face un-blinded controlled study, where single-treatment low light dose MAL-PDT and treatment with red light only were compared, no significant difference between the treatment protocols was obtained. Both MAL-PDT and red light only showed significant decrease in acne score. The studies also showed that there was no significant reduction of *P. acnes* or sebum excretion, neither for ALA-PDT nor for MAL-PDT. Furthermore, fluorescence images revealed poor selectivity of MAL-induced fluorescence to the acne lesions. In a fourth, *in vitro* study the photodynamic effect on the skin bacteria *P.acnes* was investigated. Bacteria suspensions were anaerobically incubated in the presence or absence of sensitizer, i.e. ALA or MAL. The viable counts of *P.acnes* were significantly reduced after illumination with either red or blue light when incubated in the presence of either ALA or MAL; however, long incubation times were necessary (4 to 5 days), confirmed by fluorescence measurements.

Taken together, the results of this thesis suggest that PDT using either ALA or MAL is effective in treatment of acne. Light doses minimizing side effects such as pain and hyperpigmentation should be applied. However, the results also imply that explanations other than eradication of *P. acnes* and destruction of the pilosebaceous unit should be considered for describing the mechanisms behind the treatment.

Key words: Acne Vulgaris, delta-aminolaevulinic acid, fluorescence imaging, methyl-aminolaevulinic acid, photodynamic therapy, porphyrins, Propionibacterium acnes