

Photodynamic Therapy for Treatment of Acne Vulgaris in Clinical Studies: Dose Response and Mode of Action

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Camilla Hörfelt from the Department of Dermatology and Venereology, University of Gothenburg, Sweden, defended her thesis on 2 April, 2009 at Sahlgrenska University Hospital, Gothenburg, Sweden. The opponent was Professor Hans Christian Wulf from Bisbebjerg Hospital, Denmark.

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. PDT is based on an initial photosensitization of the skin, followed by irradiation with visible light, to produce cytotoxic singlet oxygen. In the treatment of acne, PDT is thought to affect the sebaceous glands and the bacterium *Propionibacterium acnes*; however, the full mechanism is not clear. The aim of this research was to investigate the mechanisms of action and the most effective treatment regimen for PDT for acne.

Patients with mild to severe acne were included in the study. In a non-blinded 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 methyl aminolaevulinate (MAL)-PDT and placebo treatments. A greater reduction in total inflammatory lesion count was obtained with two consecutive MAL-PDT treatments compared with placebo-PDT; however, in another split-face unblinded controlled study, in which 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 a significant decrease in acne score. The studies also showed that there was no significant reduction in *P. acnes* or sebum excretion, either for ALA-PDT or 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. Bacterial suspen-



Fig. 1. Camilla Hörfelt and Professor Hans Christian Wulf (opponent).

sions were incubated anaerobically in the presence or absence of sensitizer, i.e. ALA or MAL. 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 (4–5 days), as confirmed by fluorescence measurements.

Taken together, these results 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.

List of original publications

1. Hörfelt C, Funk J, Frohm-Nilsson M, Wiegleb Edström D, Wennberg A-M. Topical methyl aminolaevulinate photodynamic therapy for treatment of facial acne vulgaris: results of randomized, controlled study. *Br J Dermatol* 2006; 155: 608–613.
2. Hörfelt C, Stenquist B, Larkö O, Faergemann J, Wennberg A-M. Photodynamic therapy for acne vulgaris: a pilot study of the dose-

- response and mechanism of action. *Acta Derm Venereol* 2007; 87: 325–329.
3. Hörfelt C, Stenquist B, Halldin CB, Ericson MB, Wennberg A-M. Single low dose red light is as efficacious as MAL-PDT for treatment of acne: clinical assessment and fluorescence monitoring. *Acta Derm Venereol* 2009; 89: 372–378.
 4. Hörfelt C, Karami N, Faergemann J, Wennberg A-M, Ericson MB. 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.