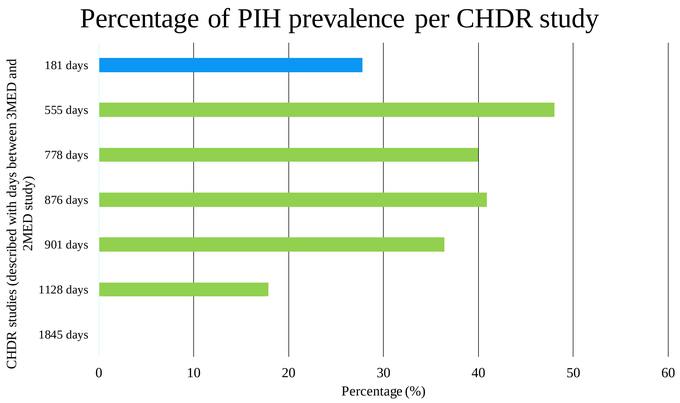
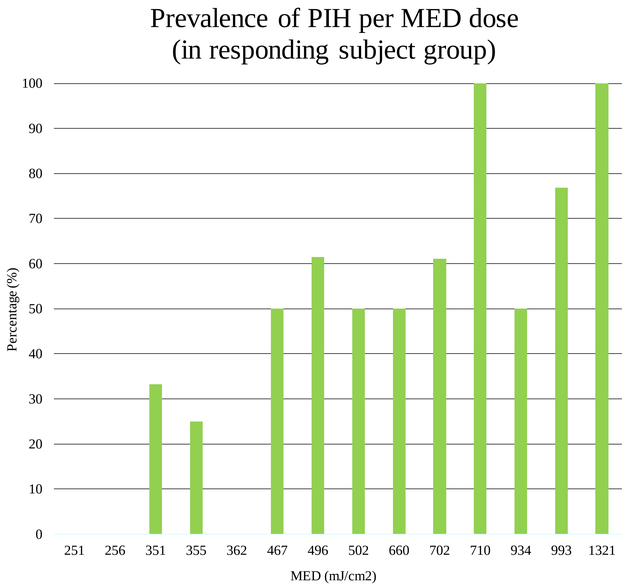
The ultraviolet-B heat pain model

Postinflammatory hyperpigmentation and validation of a 2MED dose to induce hyperalgesia in healthy subjects.

P. Siebenga, G. van Amerongen, H.J. Hijma, E.S. Klaassen, M.L. de Kam, R. Rissmann, G.J. Groeneveld
Centre for Human Drug Research, Leiden, The Netherlands





INTRODUCTION

Human evoked pain models are used to demonstrate analgesic activity and find active dose ranges, but must not cause long-term side effects. The ultraviolet-B pain model is a model for inflammatory pain. Typically, 3x minimal erythema dose (MED) is used. After several performed studies at our centre, subjects reported long-lasting hyperpigmentation on the UVB irradiated area(s). We performed a study to investigate the prevalence of postinflammatory hyperpigmentation. Additionally, we re-evaluated the ultraviolet-B heat pain model with a 2MED paradigm.

METHODS

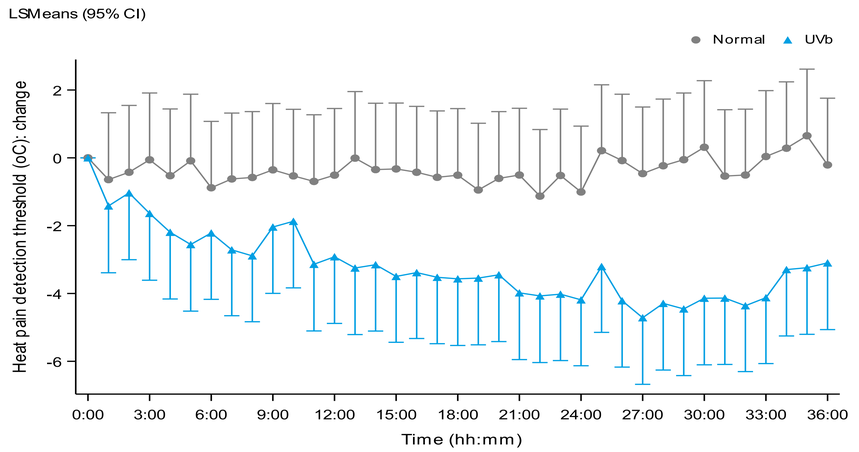
The first study was a retrospective study. All subjects ever exposed to 3MED UVB irradiation were invited for an evaluation of the exposed area(s). The second study was a safety and efficacy study in which 18 healthy subjects (9 men and 9 women) were exposed to 2MED UVB irradiation. Hourly measurements until 36 hours post-irradiation were performed with a contact heat thermode (Medoc TSA-II) assessing PDT. Comparisons were done between UVB irradiated and control skin.

RESULTS

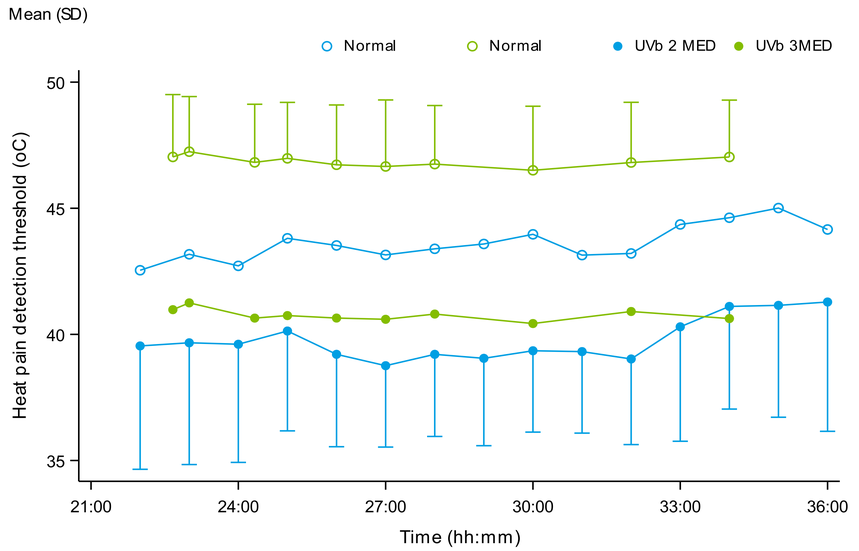
Study I: 78/142 subjects (55%) responded. The prevalence of PIH in the responding subject group was 53.8%, and in the total group 29.6%.
Study II showed a significant contrast difference between UVB exposed and control skin of the thermal pan detection threshold from 3 hours post-irradiation (estimate of the difference 1.58°C, 95% CI 0.26 – 2.90, p=0.0188) onwards and remained stable throughout the study. From 13 hours after irradiation the LSMean estimate of the difference from baseline control skin in heat PDT ranged between -2.6°C and -4.45°C (p<0.0001). After 6 months 5/18 subjects (27.8%) still had a hyperpigmentation on the back (1/5 minimal; 4/5 mild in intensity).

CONCLUSION

The 3MED model leads to a high prevalence of PIH, which, so far, has never been reported. The 2MED paradigm produced a stable hyperalgesia and minimizes the risk of PIH. More definite results on the prevalence of PIH can be revealed in 1 year.



Change from baseline graph of the least squares mean pain detection thresholds over time on the UVB irradiated area and control area.
C= Celsius; CI = Confidence Interval; LSMeans = Least square Mean; UVb = Ultraviolet-B.



Mean pain detection thresholds over time on the UVB irradiated and control area for 2MED (Study II) and 3MED (Study CHDR1422, CHDR1425, CHDR1431 and CHDR1440). Time on x-axis is the post-irradiation time.
C= Celsius; CI = Confidence Interval; MED = Minimal erythema dose; SD = Standard deviation; UVb = Ultraviolet B.

Centre for Human Drug Research | Zernikedreef 8 | 2333 CL Leiden | The Netherlands
Tel +31 71 52 46 400 | info@chdr.nl | www.chdr.nl