Fractional laser assisted photodynamic therapy in actinic keratosis: A pilot study

Published: 05-10-2012
Last updated: 17-01-2025

Objective is to perform a pilot study in order to assess wether a randomized controlled study can follow. This randomized study is necessary to proof effectiveness compared to regular photodynamic therapy. Objective is to present an effective and...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON57215

Source
ToetsingOnline

Brief title
Fractional laser assisted PDT in Actinic keratosis

Condition

- Skin neoplasms malignant and unspecified

Synonym
actinic keratosis, sun damaged skin

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Er is geen financiering voor deze pilot studie. De laser is aanwezig op onze polikliniek;het onderzoek wordt verricht door een arts-assistent die werkzaam is op de poli.

Intervention

Keyword: Actinic keratosis, Fractional ablative laser, Laser assisted photodynamic therapy, Photodynamic therapie (PDT)

Outcome measures

Primary outcome

Primaire outcome:

* Effectiveness of AFR pre-treatment in PDL laser assisted PDT for AK

* Reduction of incubation time topical PDT drugs (MAL/Metvix) with 50% using

AFR density 50%.

Secondary outcome

Secondaire outcome:

* Patient satisfaction

* Pain score (VAS)

* Complications/adverse outcomes

* Duration of treatment

* Cost of treatment

This has to be proved with a randomized controlled study later on.

Study description

Background summary

Actinic keratoses (AK) are cutanous neoplasms prevalent in up to 40% to 60% of Caucasians older than 40 years and 80% of whites older than 60 years. Presumable 0.25-1% of AK develops into a squamous cell carcinoma (SCC) yearly. The risk of developing a SCC within untreated AK can increase to 10% to 20% per decade depending on the study. The development of SCC on sun-damaged skin is a

gradual process; however, most AK lesions do not progress to invasive SCC and it currently is not possible to clinically or histopathologically determine which AK lesions will progress to SCC.
Many therapies exist, such as ablative therapies, including curettage and cryotherapy or topical chemotherapy, including topical fluorourail and imiquimod. Disadvantages of these approaches are hypopigmentation, scarring, limitation of the body surface area (BSA) and the need for a high patient compliance with topical applicants. Another category of treatment is photodynamic therapy (PDT). This is based on the concept of combining a photo-sensitizer and light, also called photochemotherapy. Photo-sensitizers that are used are 5-amniolevulinic acid (5- ALA) or methyl-aminovelunate, which are applied 3.5-4 hours before treatment under occlusion.
ALA-PDT is known to be painful for patients. A study done by Arits et al shows that pain scores in PDT are higher in subgroups with Fitzpatrick skintype I and II, lesion type AK and chronic use of oral analgesics. There was also a trend towards higher mean pain scores for subgroups aged over 70, tumour localization in the head/neck region and use of oral analgesics before PDT.
Other light sources that could be effective when combined with a photo sensitizer, in the treatment of actinic keratosis, were investigated. The absorption spectrum of protoporphyrin IX, the conversion product of 5-ALA responsible for the photodynamic reactions has a peak in the 585 nm range. In several studies study the pulsed pulsed dye laser (LP-PDL) for the treatment of AK*s and the safety and efficacy of this treatment was assessed. They concluded that this treatment is safe and effective and report minimal discomfort and excellent post treatment cosmetic results. ,
Several studies indicate that ablative fractional laserresurfacing (AFR) facilitates topically applied photosensitizers such as ALA or Metvix. AFR creates vertical channels that may facilitate topical PDT drug penetration and thereby improve PDT response in the deeper skin layers. It could then be more effective in thicker AK lesions.
Prior studies done in the field of photodynamic therapy suggest that an average incubation time of 3 hours is needed for the PDT topical drugs to reach the maximum fluorescence level. Haederhal et al. performed a study in which maximal fluorescence was reached at 1,5 hour after fractional laser treatment of pig skin. A deeper photodynamic reaction was seen, and therefore maximal fluorescence time was reduced to 50%. So far this has not been investigated in human skin.
The purpose of this pilot study is to assess whether ablative fractional laser assisted photodynamic therapy is an effective treatment for AK and can reduce incubation time of topical PDT drugs with 50% using an AFR density of 50%.

Study objective

Objective is to perform a pilot study in order to assess wether a randomized controlled study can follow. This randomized study is necessary to proof effectiveness compared to regular photodynamic therapy.
Objective is to present an effective and patient friendly treatment for

(chronic) actinic keratosis.

Study design

This is a pilot study that will take place at the department of Dermatology in the Catharina Hospital Eindhoven, the Netherlands.

Patients: Patients aged older than 30 years with clinically proven actinic keratosis on the vertex and/or forehead.

Inclusion: Patients will be included by dermatologists, dermatologic residents and a trained physician assistant after informed consent is given.

Study design:
In this pilot study we would like to investigate whether there is good response to AFR pre-treatment in laser-mediated PDT. The eventual goal will be to set up a clinical randomized trial in which the true effect of AFR in PDT has to be examined.
In this study the response will be measured using Total Lesion Number Score (TLNS), Total Thickness Score (TTS) and in follow-up visits an independent investigator will determine Investigator Global Improvement Indices Score (IGII-score).

TLNS: Total amount of actinic keratosis lesions
TTS: R = complete remission / no AK
1 = lesion is visible, not palpable
2 = lesion visible and palpable
3 = lesion elevated with visible keratosis
4 = lesion hyperkeratotic and > 1 mm thick

Investigator Global Improvement Indices (IGII):
-2 = significantly worse
-1 = little worse
0 = no improvement
1 = poor improvement
2 = little improvement
3 = significant improvement
4 = complete remission

Follow up:
All patients will be visiting the outpatient department in the following frequency:
- 10 days
- 1 months
- 3 months
During each follow-up visit colour photographs will be taken and whenever there is a new area that needs to be treated or in case of recurrence, this will be

registered clearly.

Interventions
UltraPulse, fractional CO2, Lumenis, 10.600 nm, 10 mJ/pulse, 0.12 mm spot size, 5% ablation rate 1-3 minutes of treatment duration
This laser therapy is followed by the application of a photosensitizer (MAL/METVIX). Patients will wait 1,5 hour for the photosensitizer to work. After that the illumination will be performed using the Pulsed Dye Laser (Candela, WA); 595 nm, spot diameter 7 mm; 7J/cm2, pulse duration 10 ms, 1-3 minutes of treatment duration.

Intervention

UltraPulse, fractional CO2, Lumenis, 10.600 nm, 10 mJ/pulse, 0.12 mm spot size, 5% ablation rate

Study burden and risks

Patients will undergo a short (1-3 minutes) treatment with the fractional ablative laser (UltraPulse, fractional CO2, Lumenis, 10.600 nm)This treatment will not be without any pain sensation, however the ablative fractional laser is used as treatment for other purposes aswell.
Next - comparable to regular photodynamic therapy - a photosensitizer cream will be applicated on the treatment zone.
The cream will be removed after 1,5 hour, after which illumination with the Pulsed dye laser will be performed. Merely this is assessed as painless by patients.
After treatment patients will be seen in follow-up, 10 days, 1, 2 and 3 months after treatment. Regular follow-up visits will be done afterwards (outside study).

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P. Debyelaan 25
Maastricht 6229 HX
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

P. Debyelaan 25
Maastricht 6229 HX

NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Caucasian patients > 30 years
Fitzpatrick skin type I-III
Clinically proven Actinic Keratoss on vertex and/or forehead

Exclusion criteria

Prior treatment of AK within the past 6 months
Suspicion for malignancy
Known hypersensibility for ALA/MAL photosensitizers
Use of Diclofenac gel, tretinoine cream, salicylic acid and/or topical corticosteroids in the past 6 months on vertex and/or forehead
Psoriasis and/or eczema on vertex and/or forehead

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO Date:	05-10-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	15-07-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL41207.060.12

Study results

Summary results
Trial never started