Topical application of calcipotriol for preventive treatment of hypertrophic scars: a randomized, double-blind, placebo-controlled trial

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27742

Source
NTR

Brief title
N/A

Health condition

Hypertrophic scars, keloids
Littekenhypertrofie

Sponsors and support

Primary sponsor: VU University Medical Center, Amsterdam.
This investigation was supported by a grant of the Dutch Burns Foundation and the Cornelis Visser Foundation.
Source(s) of monetary or material Support: This investigation was supported by a grant of the Dutch Burns Foundation and the Cornelis Visser Foundation. The ointment packages were provided by Leo Pharma A/S.

Intervention

Outcome measures

Primary outcome

Evaluations took place under standardized circumstances at 3 weeks, 3 months and 12 months following surgery and were performed by the same observer (IEW).
During all evaluations, the scar's clinical aspect was scored as normotrophic (when flat) or hypertrophic (when raised above surrounding skin level). Scoring and measuring was done at 3 cm from the scars lateral and medial extremes.

To quantify the scar's macroscopic properties, its thickness was measured ultrasonographically at 3 and 12 months postoperative, using a 7,5 MHz-probe (SSD-680 EX/STD, Aloka Co., Ltd., Japan). In order to obtain a reliable image, a gel pad (Aquaflex®, Parker Laboratories Inc., Fairfield, USA) was placed between the probe and the skin. The distance (in mm) between the echogenic stratum corneum and subcutaneous tissue (appearing as a 'black circle') was measured. This method has proven to be valuable in the morphological assessment of the skin, but also in distinguishing normal from hypertrophic scars.

Secondary outcome

During all evaluations 3 mm punch biopsies were collected, consecutively at 5 cm, 4 cm and 3 cm from the lateral confines of both lateral scars after local anaesthesia with 5 ml lidocaine HCL (10 mg/ml) combined with epinephrine (0.01 mg/ml).

Prior to immunohistochemical staining, the frozen biopsy samples were further processed into 5 ìm cryostat sections, embedded on glass slides. Monoclonal antibodies were used for staining the sections.

The number of epidermal layers (acanthosis) was counted in the haematoxylin-eosin stained sections. The percentage of proliferating basal keratinocytes was evaluated in anti-Ki-67 stained sections, by counting both the total number of basal keratinocytes (heamatoxilin-stained) and the number of Ki-67-positive basal keratinocytes. The presence or absence of activated keratinocytes was evaluated in anti-keratin-16 stained sections, by scoring suprabasal staining as absent or present. The percentage of epidermal Langerhans cells was calculated using computer-assisted microscopic evaluation using NIS-Elements AR, version 2.3 (Nikon Inc.). After a representative part of the epidermis was outlined, running from basal membrane to stratum corneum, the surface area of CD1a-positive tissue within the selection was expressed as a percentage of the total area in the selection.

Study description

Background summary

Background.

The epidermis of hypertrophic scars shows histological abnormalities similar to psoriatic lesions. Calcipotriol is widely used for treatment of psoriasis.

Objectives.
To investigate the efficacy of topical application of calcipotriol in preventing hypertrophic scar formation.

Methods.
In a randomized, double-blind, placebo-controlled trial, 35 women were enrolled. The bilateral reduction mammoplasty wound healing model was used. Starting 10 days postoperative, scar-segments were either treated with calcipotriol or placebo, for the total duration of three months. At 3 weeks, 3 months and 12 months postoperative, the scar aspect was scored, its thickness was measured by ultrasound, and punch biopsies were collected for histological analysis.

Results.
After 3 and 12 months, no significant difference in prevalence of hypertrophic scars was observed between the placebo- and calcipotriol-treated scars. At 3 weeks postoperative, the calcipotriol-treated scars contained significantly more epidermal layers ($p=0.017$) and proliferating basal keratinocytes ($p=0.029$). None of the 3-week-old scars without activated keratinocytes became hypertrophic, whereas 48% of the 3-week-old scars that contained activated keratinocytes did ($p=0.001$). After three months, hypertrophic scars contained more epidermal layers than normotrophic scars ($p=0.013$).

Conclusions.
Topical application of calcipotriol during the first three months of wound healing did not affect the incidence of hypertrophic scar formation. Contrary to its effects in psoriatic lesions, calcipotriol treatment increased proliferation of keratinocytes and the number of epidermal layers. We observed a strong association between keratinocyte activation and hypertrophic scar formation. These findings contribute to the concept of both dermal and epidermal involvement in the aetiology of hypertrophic scar formation.

Study objective

The epidermis of hypertrophic scars shows histological abnormalities that are similar to

psoriatic lesions. Calcipotriol is widely used for treatment of psoriasis. We investigated the efficacy of topical application of calcipotriol in preventing hypertrophic scar formation.

Study design

Evaluations took place under standardized circumstances at 3 weeks, 3 months and 12 months following surgery and were performed by the same observer (IEW).

Intervention

Ten days following surgery (after reepithelialization had been established), participants received a pair of ointment packages, marked ‘R’ and ‘L’, which were kindly provided by Leo Pharmaceutical Products (Ballerup, Denmark).
These were randomly filled with either calcipotriol 50 ìg/g (Daivonex® in vehicle) or placebo (vehicle only).

Both participant and observer were unaware of the content of the ointment packages. Participants were carefully instructed to apply the content of the package marked ‘R’ with the right hand on the left lateral (LL) and right medial (RM) scars. Accordingly, the content of the package marked ‘L’ had to be applied on the right lateral (RL) and left medial (LM) scars. The application frequency was twice daily, with a total duration of three months.
To verify our data, participants were questioned during the last evaluation about the way the ointment had been applied. This resulted in a minor adaptation of data in one case, as the ointment had been applied oppositely. Not until the final evaluation of the last participant, the key to the exact content of the packages was revealed and inserted into the data file.

Contacts

Public
VU University Medical Center
Department of Plastic and Reconstructive Surgery
PO Box 7057
F.B. Niessen
Amsterdam 1007 MB
The Netherlands
+31 (0)20 4443261
Scientific
VU University Medical Center
Department of Plastic and Reconstructive Surgery
PO Box 7057
F.B. Niessen
Amsterdam 1007 MB
The Netherlands
+31 (0)20 4443261

Eligibility criteria

Inclusion criteria

Women aged above 18 years that were planned for bilateral reduction mammoplasty at the University Medical Center of Groningen received written information about the study prior to surgery.

Exclusion criteria

Exclusion criteria for participation were current or planned pregnancy in the first year following surgery and postoperative complications (e.g. haematoma, infection).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2002
Enrollment:	35
Type:	Actual

Ethics review

Positive opinion

Date:	09-10-2008

Application type: First submission

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
NTR-new	NL1427
NTR-old	NTR1486
Other	Dossiercode METC AZG : 2000/168
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A