Does local application of betamethasonvalerate 0.1% cream twice a day reduce the complaints of chronic chilblains?

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Research question:Does thin application of betamethasonvaleraat cream 0,1% on perniones lesions twice a day reduce the symptoms of patients as determined in 1st. line health care, with at least 10 mm expressed on a visual analogue scale, together…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders NEC
Study type	Interventional

Summary

ID

NL-OMON34743

Source
ToetsingOnline

Brief title
BCCC

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
Chronic Chilblains

Research involving
Human

Sponsors and support

Primary sponsor: Huisartspraktijk Souwer

Source(s) of monetary or material Support: ZonMw fonds alledaagse ziekten;projectnummer 4201.1006.

Intervention

Keyword: Betamethason cream, Chilblains, RCT, Therapy

Outcome measures

Primary outcome

We consider the intervention effective if a reduction of the experienced complaints or is discovered, displayed in a decline of the score "complaint" with at least 10 mm on the visual analogue scale concerned. "Complaint" is defind as Max (itch,pain): the Vas score for or itch or pain, depending on the highest score.

Secondary outcome

Secondary we register scores for impairement and the experienced side effects, skin irritation, and symptoms of skin atrophy: purpurae, inclination to bleed and depigmentation.

Study description

Background summary

Chilblained hands, toes and thighs form an acute and clinical picture labelled as perniones. Chronic perniones is a nasty and painful disorder often returning every winter and can cause considerable limitations in every day life (1,2).
Little is known about nature and treatment. There is uncertainty about incidence and prevalence. Data of the Continual Morbidity Registration point to four new cases per GP per year, mostly women (3). Prevalence is probably significantly higher, also in our experience sofar.
There is limited evidence for three interventions: Vitamin D3, nifedipine and corticosteroïd cream (4).
We have already proven the unlikeliness of a positive effect of Vitamin D3 (5).
Indications for possible positve effects of a corticosteroïd creme are

described in only one publication with a case series of 20 participants and therefore aren't very strong (6).
As patients with perniones do have a need for effective treatment to relieve them from their complaints and limitations (2), we are of the opinion that it is useful to further investigate the possible effectiveness of corticosteroïd cream.

References:
1. Souwer IH, Lagro-Janssen ALM. Perniones. Winterhanden, Wintertenen en *Winterdijen*. HuisartsWet
2004;47:594-6.
2. Souwer IH, Robins LJH, Lagro-Janssen ALM. Chilblains from the patient*s perspective. Eur J Gen
Pract. 2007;13:159-60.
3. Continue Morbiditeit Registratie Nijmegen: unpublished data.
4. Souwer IH, Lagro-Janssen ALM. De behandeling van perniones. Een literatuuronderzoek. Huisarts
Wet 2004;47:561-2.
5. Souwer IH, Lagro-Janssen ALM. Vitamin D3 is not effective in the treatment of chronic chilblains. Int
J Clin Pract 2009;63:282-6.
6. Ganor S. The treatment of chilblains with fluocinolone cream under occlusive dressing. Harefuah
1973;84:163.

Study objective

Research question:

Does thin application of betamethasonvaleraat cream 0,1% on perniones lesions twice a day reduce the symptoms of patients as determined in 1st. line health care, with at least 10 mm expressed on a visual analogue scale, together with a good tolerancy of the medication.

Study design

This research has been set up as RCT of the cross over type. A group of 50 perniones patients is randomised over two sub groups. After one week of baseline measurements withhout intervention, they are treated with betamethason cream or a placebo cream for 6 weeks in turns, blindfold to patient and researcher.

The duration of the research is 13 weeks for each patient. The most important confounder, exposure to cold, is monitored by asking for the twenty-four hours data of "de Bilt" at the KNMI and specific questions at intake.

Informed consent.
Participants are included in the study after informed consent only. All required information, written and oral, will be provided to the potential participant in the initial interview and is also incorporated in the diary that is kept up to date by the participant during the research .

Procedure and randomisation.
After application an intake interview takes place. The diagnosis is then confirmed by the researcher. It is checked whether the participant satisfies the inclusion criteria and should not be rejected on basis of the exclusion criteria.
After informed consent the lesions are documented by means of description and fotos. Additional information is gathered about the way of dressing, exposure to cold, housing conditions and working environment.
Randomisation takes place over two regimes by means of *permuted block randomisation* with a block size of 10.
Regime 1: 1 week - no medication; 6 weeks - placebo cream locally twice a day and 6 weeks - betamethasonvaleraat cream 0,1% locally twice a day.
Regime 2: 1 week - no medication; 6 weeks - betamethasonvaleraat cream 0,1% locally twice a day and 6 weeks - placebo cream locally twice a day. The research medication is provided in tubes of 15 grammes, one for each week of research.

Measuring instrument.
The measuring instrument is a diary kept up to date daily by the participant for the complete research period.
Per day, experienced complaints of perniones (itch or pain), experienced limitations in daily life, experienced headache, experienced dizziness and experienced general indisposition are scored on a 100 mm visual analogue scale.
For the complete research period of each individual patient the exposure to cold is registered by asking for the average day temperature as measured in "de Bilt" at the KNMI.
There are 6 contact moments: intake (t1), end of week 1 (t2), end of week 4 (t3), end of week 7 (t4), end of week 10 (t5) and end of week 13 (t6). Control and correction on completeness of the diary and consistency of the therapy used is performed by weighing the used tubes.

Primary result measurement.
We consider the intervention effective if a reduction of the experienced complaints or is discovered, displayed in a decline of the score "complaint" with at least 10 mm on the visual analogue scale concerned. "Complaint" is defind as Max (itch,pain): the Vas score for or itch or pain, depending on the highest score.

Secondary we register scores for impairement and the experienced side effects, skin irritation, and symptoms of skin atrophy: purpurae, inclination to bleed

and depigmentation.

Analysis.
A statistical analysis will be performed with a repeated measures mixed effects model. The effect of a possible change in temperature will be taken into account. An intention to treat analysis will take place. A check on the consistent use of the therapy will be done by weighing the used tubes.

Power measurement.
In previous research we found baseline VAS scores for complaint of 27.97 millimeter (SD 18.82mm) on average We regard the intervention effective when the VAS score has dropped by 10 millimeter or more. For the power measurement we took a paired T-test as a baseline. With one measurement per person for medication and placebo this is a considerable simplification of the real test. Repeated measurements allow less participants, which is more favourable.
At alpha =0.05, beta=0.10 (power 90%) and an effect of 10mm VAS 38patients are required to show a significant difference between the treatment with betamethason cream and the placebo.

Numeric Results for One-Sample T-Test
Null Hypothesis: Mean0=Mean1 Alternative Hypothesis: Mean0<>Mean1
The standard deviation was assumed to be known.
Power N Alpha
Beta Mean0 Mean1 Sigma
0.90583 38 0.05000 0.09417
27.97 17.97 18.82

Intervention

The intervention which is compared to the placebo consists of the thin application of betamethasonvaleraat cream 0,1 % twice a day for 6 weeks where the perniones laesions are located .

Study burden and risks

After application an intake interview takes place. The diagnosis is then confirmed by the researcher. It is checked whether the participant answers to the inclusion criteria and should not be rejected on basis of the exclusion criteria.
After informed consent the lesions are documented by means of description and fotos. Additional information is gathered about the way of dressing, exposure to cold, housing conditions and working environment.

Randomisation takes place over two regimes by means of *permuted block randomisation* with a block size of 10.
Regime 1: 1 week - no medication; 6 weeks - placebo cream locally twice a day

and 6 weeks - betamethasonvaleraat cream 0,1% locally twice a day.
Regime 2: 1 week - no medication; 6 weeks - betamethasonvaleraat cream 0,1% locally twice a day and 6 weeks - placebo cream locally twice a day. The research medication is provided in tubes of 15 grammes, one for each week of research.
The measuring instrument is a diary kept up to date daily by the participant for the complete research period. Experienced perniones complaints (itch or pain) and limitations in daily life are scored daily.

For the complete research period of each individual patient the exposure to cold is registered by asking for the average day temperature as measured in "de Bilt" at the KNMI.
There are 6 contact moments: intake (t1), end of week 1 (t2), end of week 4 (t3), end of week 7 (t4), end of week 10 (t5) and end of week 13 (t6). Control and correction on the completeness of the diary and the consistency of the therapy used is performed by weighing the used tubes.

We do not expect any side effects of the creams used.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

18 years or older; able to understand and follow instructions; Complaints of chronic pernio for at least 3 weeks at inclusion: itching or painfull blue-red discolorated laesions at fingers and/or toes, other lokalisations at the feet or lateral side of the thigs ("the Kibes"). The laesions may be swollen ans ulceration may be pressent but not obligitory. Onset of complaints is in the period november to februari.

Exclusion criteria

Known inflamatory disease (RA, SLE et cetera); pregnancy; lactation; actual use of a calcium antagonist, use of corticosteroÃ¯d containing cream in the past four weeks, skin defects at the skinparts to treat.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2010
Enrollment:	50

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Niet van toepassing
Generic name:	Betamethasonvalerate 1mg/g PCH cream
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	niet van toepassing
Generic name:	Cetomacrogol cream FNA
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	24-12-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-04-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2009-016664-37-NL
CCMO	NL30695.091.09
Other	NTR TC=2171