Standard Topical Ointment or Doxepin against pruritus in burn patients

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to evaluate whether Doxepin hydrochloride 5% cream versus a placebo cream significantly reduces pruritus in burn patients by comparing itch scores.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON45341

Source
ToetsingOnline

Brief title
2-STOP trial

Condition

- Epidermal and dermal conditions

Synonym
Itch, pruritus

Research involving
Human

Sponsors and support

Primary sponsor: Vereniging Samenwerkende Brandwondencentra Nederland
Source(s) of monetary or material Support: Nederlandse Brandwonden Stichting

Intervention

Keyword: Burns, Doxepin, Itch, Pruritus

Outcome measures

Primary outcome

The main study parameter is the change in pruritus intensity as measured by the Visual Analogue Scale (VAS), with a decrease of *2 point being defined as clinically significant. If the patient has more than one burn wound area (for example leg and arm) that itches, the area that causes the moist complaints will be designated as the study area. There can only be one study area.

Secondary outcome

The secondary study parameters include the determination of the MIC (Minimal Important Change) of the itch scores, the characteristics and impact of itch as measured by the BIQ (Burn Itch Questionnaire), and scar quality as measured by the POSAS (Patient and Observer Scar Assessment Scale).

Other study parameters include: the use of hydrating cream, use of escape medication and use of pressure garments. Furthermore, we will register sex, age, medical history, cause of burn, location of burn wound, %TBSA burned, time to wound healing (will be estimated retrospectively), % burn wound area that itches, duration of itch, itch before inclusion and wound treatment (conservative or surgery).

Study description

Background summary

Pruritus is a common and impairing problem in patients after burn injury, with prevalence rates up to 87%. Pruritus impairs quality of life by causing stress,

affecting mood and cognition and can give difficulty sleeping. It is associated with several risk factors. Up to three months post burn, complaints of itch were predicted by female sex, number of surgical procedures, percentage Total Body Surface Area burned (%TBSA) and post-traumatic stress symptoms, as measured by the Impact of Event Scale (IES) two weeks post burn.

The mechanism of pruritus is complex and to a large extent unknown. It involves both peripheral and central factors. The best described mediator of peripheral origin is histamine. Histamine is released during acute inflammation and in granulation tissue (formed as a by-product of collagen production) which might explain the presence of pruritus in the early phases of wound healing. Antihistamines, which by agonising histaminic receptors, have therefore been the standard of care (SOC) in the treatment of pruritus in patients after burn injury.

Doxepin is a dibenzoxepin tricyclic compound used for the treatment of depression. In 1994 topical Doxepin hydrochloride 5% was marketed for the treatment of pruritus due to eczema. The complete working mechanism of Doxepin is not known, but one of the mechanisms is the antihistaminic effect. Doxepin has an antihistaminic potent against H1 and H2 receptors, more than 50-800 times higher than other known antihistaminic agents.
In several studies by Demling, Doxepine significantly reduced itch in burn patients. However, these studies included a subpopulation of burn patients and no placebo cream was used.

Study objective

to evaluate whether Doxepin hydrochloride 5% cream versus a placebo cream significantly reduces pruritus in burn patients by comparing itch scores.

Study design

This is a multicentre, double-blind, randomized, placebo-controlled cross-over trial.

Intervention

Crossover study: patients will receive both the Doxepin cream as well as the placebo cream. With which cream they will start will bed decided through randomisation. Three phases:
1. Two weeks cream A
2. One week: wash out period
3. Two weeks cream B

Study burden and risks

The treatment period will be five weeks in total. Patients will visit the outpatient clinic after these 5 weeks. During the two times two week treatment period, patients are required to keep a diary in which they have to score their itch, and describe side effects, whether they use pressure garments and other creams or escape medications. Patients are required to fill in the Burn Itch Questionnaire after each two-week treatment with a cream and before inclusion (a total of three times).

Patients might benefit from participating as the expectation is that Doxepin cream relieves itch. Reported risks for Doxepin hydrochloride 5% cream include the development of an allergic contact dermatitis and toxicity in case of topical overdose. Application of Doxepin cream might give some stinging. A possible side effect is somnolence, especially in the first few days. Several cases of allergic contact dermatitis have been reported and care should be taken in long-term users. It is advised Doxepin cream application should be limited to a TBSA of no more than 10%. In one case-report, a ninety-year-old woman developed bullous pemphigoid after using Doxepin cream for 20 days for complaints of itch. The symptoms diminished after doxepin was stopped. Systemic effects which have been observed with orally administered doxepin (e.g. depression) are rarely observed with topical Xepin. These may include anticholinergic reactions (dry mouth, changes in taste, dry eyes, blurred vision, urinary retention), central nervous system effects other than drowsiness (headaches, fever, dizziness) and gastro-intestinal effects (nausea, indigestion, vomiting, diarrhea or constipation)

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

* Age * 18 years
* Healed burns
* Itch with an intensity * 3 as determined by the VAS score for itch at time of the enrolment
* Treatment in one of the three Dutch burn centres
* Total area that itches must not exceed >10% TBSA

Exclusion criteria

* Unable to give informed consent
* Unable to understand and fill in VAS scores and questionnaires (as determined by the treating burn physician)
* Cutaneous or systemic disease causing itch
* Any diseases or condition that is associated with adverse effects using Doxepin, that is:
o Contra-indications:
* Hypersensitivity to any of its components
o Precautions:
* Glaucoma
* A tendency to urinary retention
* Sever liver disease
* Mania
* Sever heart disease (including cardiac arrhythmias)
* Pregnancy and lactation

Study design

Design

Study phase:	4
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):	29-06-2017
Enrollment:	27
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Xepin
Generic name:	Doxepin hydrochloride 5%

Ethics review

Approved WMO

Date:	22-02-2017
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)

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	EUCTR2016-003862-25-NL
CCMO	NL59341.094.16