Enrichment randomized double-blind, placebo-controlled cross-over trial with PHEnytoin cream in patients with painful chronic idiopathic axonal polyNEuropathy

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21286

Source
NTR

Brief title
EPHENE study

Health condition

Chronic Idiopathic Axonal Polyneuropathy (CIAP)

Sponsors and support

Primary sponsor: University Medical Center Utrecht, the Netherlands
Source(s) of monetary or material Support: Prinses Beatrix fonds

Intervention

Outcome measures

Primary outcome

The primary endpoint is the change in pain intensity from baseline NRS to the mean NRS in

the second week in DOBRET positive participants.

Secondary outcome

The main secondary parameters are various other parameters of changes in pain intensity and pain characteristics, quality of life, participant's impression of change/analgesic effect, catastrophizing, side effects, use of escape pain medication, detection of plasma phenytoin levels, predictive value of the DOBRET, carry-over effects, onset and duration of analgesic effect and number daily cream applications.

Study description

Background summary

Rationale: Chronic idiopathic axonal polyneuropathy (CIAP) is a slowly progressive distal symmetric sensory or sensorimotor axonal polyneuropathy without a known cause. Approximately one-third of patients with CIAP have neuropathic pain. Until now, no randomized controlled trials have been conducted in (painful) CIAP. Neuropathic pain can be very debilitating and influences the quality of life considerably. For most patients current treatments have insufficient pain reducing effects, and/or give rise to considerable side effects. Therefore, long-term compliance is low (~45%). New treatment strategies are needed to improve neuropathic pain management. Phenytoin cream could fulfil this need.

Objectives: The main objective is to evaluate the efficacy and safety of phenytoin cream in patients with neuropathic pain due to CIAP ('painful CIAP'). The second objective is to determine the predictive value of a double-blind placebo-controlled response test (DOBRET) to identify sustained responders.
Study design: This is an enrichment randomized double-blind, placebo-controlled cross-over trial with phenytoin cream in 72 participants with painful CIAP (EPHENE study) with a duration of 6 weeks. At baseline a DOBRET with phenytoin 10% and placebo cream will be performed in each study participant to stratify participants according to their response to the DOBRET before entering the double-blind cross-over phase. DOBRET positive participants are those who experience within 30 minutes at least two points pain reduction on the 11-point numerical rating scale (NRS) on the phenytoin 10% cream applied area and at least one-point difference in pain reduction on the NRS between phenytoin 10% and placebo cream applied area, in favour of the former.
For the randomized cross-over trial phase, 48 DOBRET positive participants will enter the DOBRET positive group and 24 DOBRET negative participants the DOBRET negative group. Participants will receive in a double-blind fashion a randomized order of the three treatments: phenytoin 10%, phenytoin 20% and placebo cream. The duration of each treatment period is two weeks. Participants will cross-over two times to each of the other treatments. The study does not have wash-out periods between treatments, because the mean duration of analgesic effect after an application is expected to be less than nine hours. A blood sample will be collected at the end of the second week of the first treatment period to test for

phenytoin plasma levels.
Study population: We aim to include 72 participants, age 40 years or older, who have been diagnoses with painful CIAP at the UMC Utrecht who fulfil the inclusion criteria and have given written informed consent.

Interventions: Phenytoin cream in concentrations of 10% and 20% compared to placebo cream.

Main study parameters/endpoints:
The primary endpoint is the change in pain intensity from baseline NRS to the mean NRS in the second week in DOBRET positive participants.
The main secondary parameters are various other parameters of changes in pain intensity and pain characteristics, quality of life, participant's impression of change/analgesic effect, catastrophizing, side effects, use of escape pain medication, detection of plasma phenytoin levels, predictive value of the DOBRET, carry-over effects, onset and duration of analgesic effect and number daily cream applications.

Burden, risks and possible advantages of study participation: Burden of study participation consists of time needed to complete questionnaires and keep a daily pain diary, three extra hospital visits and one venipuncture for detection of phenytoin in plasma after the second treatment week (T1). The risks are minimal, because we do not expect clinically relevant side effects from the intervention and there is only once a minimally invasive procedure (venipuncture). The advantage of study participation is that participants can experience within a short timeframe if 10% and/or 20% phenytoin cream has a clinically relevant analgesic effect (personalized medicine).

Study objective

The main objective is to evaluate the efficacy and safety of phenytoin cream in patients with neuropathic pain due to CIAP

Study design

end of study

Intervention

Phenytoin 10% & 20% cream, placebo cream

Contacts

Public
Institute for Neuropathic Pain
David Kopsky

+31-6-28671847
Scientific
Institute for Neuropathic Pain
David Kopsky

+31-6-28671847

Eligibility criteria

Inclusion criteria

• Age 40 years or older
• Patients have been diagnosed with CIAP defined as:26 presence of symmetrical distal sensory or sensorimotor symptoms such as numbness, pins and needles, tightness, coldness, unsteadiness, muscle cramps, and weakness with onset in the feet, compatible with polyneuropathy; presence of symmetrical distal sensory or sensorimotor signs with evidence of large nerve fiber involvement such as decreased sense of touch, vibration, and proprioceptive, usually in the presence of decreased pin prick/temperature sense, decreased/absent tendon reflexes, or slight muscle weakness on neurologic examination, compatible with polyneuropathy; an insidious onset and slow or no progression of the polyneuropathy over the course of at least 6 months; no identifiable cause for the polyneuropathy after thorough history-taking, clinical examination, and extensive laboratory testing; no suggestion of a hereditary polyneuropathy based on detailed kinship history (i.e., one or more affected family member), neurologic examination, or confirmation by genetic analysis; and nerve conduction studies excluding a demyelinating polyneuropathy and confirming large nerve fiber involvement if the findings on neurologic examination are equivocal considering the patient's age.
• Presence of chronic localized neuropathic pain due to CIAP
• Neuropathic pain localized in two anatomically symmetrical areas of feet/lower legs
• Duration of neuropathic pain ≥3 months
• Duration of ≥1 hour neuropathic pain per day
• Neuropathic pain characteristics defined by a DN4 score ≥4 27
• Mean pain score of ≥4 and <10 on the NRS at study entry (baseline)
• Difference of pain intensity between left and right foot and/or lower leg of not more than 1 point on the NRS
• No changes in neuropathic pain medication for at least 1 month
• Absence of any of the exclusion criteria outlined below

Exclusion criteria

• Painful (poly)neuropathy other than CIAP
• Presence of neuropathic pain due to any other condition than CIAP

• Neuropathic pain (distribution, duration, characteristics, intensity) not fulfilling the inclusion criteria
• Pregnancy or planned pregnancy in the study period (will only be asked)
• Use of oral phenytoin
• Open wounds in the neuropathic pain area
• Current use of topical analgesics
• Presence of other pain syndromes such as the widespread pain syndrome or pain in joints
• Presence of serious psychological/psychiatric morbidity
• Addiction to intoxicants
• Hypersensitivity to the study medication (active substance and excipients)
• Insufficient mastery of the Dutch language
• Cognitive impairment and insufficiently capable to understand the purpose of the study

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2020
Enrollment:	72
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

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	NL8713
Other	METC Utrecht : 20/383

Study results