Determinants of Ectopic Calcification in Pseudoxanthoma Elasticum and Healthy controls:
Evaluation of their Relations

Published: 09-11-2016
Last updated: 19-08-2024

The main objective of this study is to compare calcification promoting and inhibiting factors and their interactions in the serum of PXE patients and healthy controls. Secondary objectives (optional) are:1) to identify differences in cognitive...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON47548

Source
ToetsingOnline

Brief title
DECIPHER study

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders
- Skin and subcutaneous tissue disorders NEC
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Pseudoxanthoma Elasticum

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Vrienden van UMC

Intervention

Keyword: Biomarkers, Medial arterial calcification, Pseudoxanthoma Elasticum

Outcome measures

Primary outcome

Differences in serum levels of calcification promoting and inhibiting factors

between PXE patients and healthy controls.

Secondary outcome

1) differences in MRI brain lesions, vascular brain flow pulsatility and brain

tissue perfusion between PXE patients and healthy controls.

2) to link these differences to differences in cognitive function.

3) differences in retinal and choroidal structures and functional outcome in

PXE patients and healthy controls

4) differences in visus related QoL in PXE patients and healthy controls

Study description

Background summary

PXE is a monogenetic disease associated with calcification of the soft tissues including the medial arterial layer. Medial arterial calcification (MAC) is associated with increased cardiovascular risk. Recent evidence suggests an association between PXE and cognitive disorders at a relatively young age. Recently, inorganic pyrophosphate has been identified as an important factor in the pathogenesis of PXE, but other circulating calcification factors also appear to be dysregulated. How these circulating factors relate to each other has never been studied. Therefore, this study aims to identify differences in calcification promoting and inhibiting factors in the serum of PXE patients

compared to healthy controls. This might give more insight in the pathophysiology of MAC in general and PXE in particular and might eventually lead to new clues for treatment possibilities and more disease specific treatment. Secondary aims of this study are 1) to identify differences in cognitive disorders and MRI abnormalities in PXE patients and healthy controls and 2) differences in retinal and choroidal structures and functional outcome and visus related quality of life in PXE patients and healthy controls

Study objective

The main objective of this study is to compare calcification promoting and inhibiting factors and their interactions in the serum of PXE patients and healthy controls.
Secondary objectives (optional) are:
1) to identify differences in cognitive disorders and MRI abnormalities in PXE patients and healthy controls
2) to identify differences in retinal and choroidal structures and functional outcome and visus related quality of life in PXE patients and healthy controls.

Study design

patient control study

Study burden and risks

The serum of 74 PXE patients has already been collected for the measurement of calcification promoting and inhibiting factors for the TEMP study (METC nr 15/125; NL47602.041.15). However, a healthy control group is lacking.
Blood from additional PXE patients and healthy controls will be collected by venepunctures. Aside from the normal risks of these venepunctures (hematoma formation, tenderness and swelling of the puncture side, persistent bleeding and vasovagal response) no potential health risks are assumed.
To investigate the brain involvement in PXE patients, brain MRI*s of 21 PXE patients participating in the TEMP trial have been made at baseline. Partners of these PXE patients will be approached to undergo brain MRI and cognitive testing. The MRI with gadolinium yields no additional risk. We exclude patients with renal insufficiency and therefore we do not expect the occurrence of nephrogenic systemic fibrosis. Research participants gain no individual benefit from their participation in this study

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

For PXE patients:
1. Age 18 and older.
2. Clinical diagnosis of PXE. For the present study the revised criteria for diagnosis of PXE from Plomp et al. (2010) will be used. At least two (or more) criteria not belonging to the same (skin, eye, genetic) category should be present for inclusion.
a. Skin
i. Yellowish papules and/or plaques on the lateral side of the neck and/or flexural areas of the body
or
ii. Increase of morphologically altered elastin with fragmentation, clumping and calcification of elastic fibers in a skin biopsy taken.
b. Eye
i. Peau d'orange of the retina; or
ii. One or more angioid streaks (AS), each at least as long as one disk diameter. When in doubt, fluorescein or indocyanine green angiography of the

fundus is needed for confirmation.
c. Genetics
i. A pathogenic mutation of both alleles of the ABCC6gene
ii. A first-degree relative (parent, sibling or child) who meets independently the diagnostic criteria for definitive PXE, For healthy controls:
1. Age 18 and older

Exclusion criteria

For PXE patients:
1. Subjects who are unable or unwilling to sign an informed consent., For healthy controls:
1. Subjects who are unable or unwilling to sign an informed consent.
2. Two or more criteria for diagnosis of PXE from Plomp et al. (2010), Additional exclusion criteria for participation in the brain MRI study:
3. Severe renal impairment (estimated creatinine clearance/eGFR of <30 ml/min/1.73m2 calculated using CKD-EPI equation).
4. A pacemaker
5. A metallic foreign body in the eye
6. Severe claustrofobia

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-12-2016
Enrollment:	126
Type:	Actual

Ethics review

Approved WMO Date:	09-11-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-10-2019
Application type:	Amendment
Review commission:	METC NedMec

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	NL58514.041.16