Renal involvement in chronic progressive external ophthalmoplegia

Published: 22-03-2007
Last updated: 08-05-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON30688

Source
ToetsingOnline

Brief title
Renal involvement in CPEO

Condition

- Musculoskeletal and connective tissue disorders congenital
- Inborn errors of metabolism
- Renal disorders (excl nephropathies)

Synonym
chronic progressive external ophthalmoplegia, Kearns-Sayre syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: chronic progressive external ophthalmoplegia, kidney, mitochondria, renal failure

Outcome measures

Primary outcome

The prevalence of renal dysfunction in CPEO patients

Secondary outcome

The prevalence of polyneuropathy in CPEO patients and the correlation between

polyneuropathy and renal dysfunction

Percentage of heteroplasmy in blood en urine sediment

Study description

Background summary

Chronic Progressive External Ophthalmoplegia (CPEO) is a rare disease, which is characterized by a slowly progressive weakness of the extraocular muscles. CPEO is a mitochondrial disorder, which means that the symptoms result from a defect in the intracellular energy production.
Mitochondria contain a unique stand of mitochondrial DNA (mtDNA); most cases of CPEO are caused by a mutation in this mtDNA. In mitochondrial disorders, normal mtDNA commonly coexists with mutant mtDNA within each cell. This is called heteroplasmy. A higher percentage of heteroplasmy means relatively more mutant mtDNA and often more severe symptoms. The percentage of heteroplasmy (and therefore the chance of finding a mutation) is commonly highest in skeletal muscle, which is obtain through a muscle biopsy.

All cells contain mitochondria and therefore CPEO commonly causes involvement of other organs, mainly those with a high energy demand (skeletal muscle, brain, peripheral nerves and heart). Kidney*s also have a high energy demand and indeed several case report mention renal involvement in mitochondrial disorders including CPEO. The exact prevalence of renal failure in CPEO has never been studied yet.

Polyneuropathy is a common feature of CPEO. Commonly it is attributed to the

direct effect of mitochondrial dysfunction on peripheral nerve function.
However, in the general population, a common cause of polyneuropathy is renal failure.

Study objective

The goal of this study is to answer the following questions:

1. Is the chance of detecting mtDNA mutations in blood or urine sediment as high as in a (much more invasive) skeletal muscle biopsy sample?

2. What is the prevalence of renal failure in CPEO?

3. Is there a correlation between the prevalence of polyneuropathy and renal failure in CPEO

Study design

All 40 patient, who were previously diagnosed in the Radboud University Nijmegen Medical Centre with CPEO according to the clinical criteria, will be invited to participate. If the patient is willing to participate, the investigator mails the patient a container for collecting urine. Furthermore the investigator will visit the patients at home for:

• taking medical history to evaluate the use of medication, which can influence renal function as well as a possible family history of renal disease
• venipuncture for collection of blood sample
• measuring blood pressure
• measuring achilles tendon reflex and sense of vibration

Study burden and risks

The only significant burden associated with this study is the venipuncture; adverse effect as a result of this are highly unlikely.
Genetical tests are only performed in patients, in whom the muscle biopsy already revealed a pathogenic mtDNA mutation. This excludes the possibility that patients will unwittingly receive a new genetical diagnosis.

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

CPEO according to clinical criteria

Exclusion criteria

none

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2007
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

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
CCMO	NL15532.091.07