Validation of athe conchotome percutaneous technique to perform a muscle biopsy to measure biochemical parameters in mitochondrial disease

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Primary objective:The validation of the conchotome percutaneous muscle biopsy to measure ATP production in patients suspected of mitochondrial disease.Secondary objectives:The validation of the conchotome percutaneous muscle biopsy to measure…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Inborn errors of metabolism
Study type	Observational invasive

Summary

ID

NL-OMON34211

Source
ToetsingOnline

Brief title
Validation of the conchotome percutaneous muscle biopsy

Condition

- Inborn errors of metabolism

Synonym
energy metabolism disturbance, mitopathy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: AGIKO van ZonMW

Intervention

Keyword: biochemical analysis, mitochondrial disease, muscle biopsy

Outcome measures

Primary outcome

Primary outcome parameter

ATP production in muscle

Secondary outcome

Substrate oxidation rates in muscle cells

Enzyme complex activities in muscle cells

Complications of muscle biopsy

Study description

Background summary

Mitochondrial diseases are disorders in which energy metabolism is disturbed. Patients with these conditions may present with a variety of symptoms from different organs. This makes it difficult to make a diagnosis on clinical grounds.

The diagnosis of mitochondrial disease is based on the analysis of energy production (ATP), processing sugar (substrate oxidation rates) and the activity of different enzyme complexes of the respiratory chain in muscle cells. These muscle cells are obtained by a piece of muscle removed by an open muscle biopsy of the musculus vastus lateralis. This requires children a day are included and are placed under general anesthesia. With this study we want to see if it is possible with a less invasive technique to obtain muscle cells in which the various biochemical processes can be studied.

In Sweden and England, standard biopsies are obtained from the tibialis anterior muscle under local anesthesia.
This less invasive technique would have several advantages over the open muscle biopsy. Children no longer need to be anesthetized. It is known that children

with mitochondrial disease have an increased sensitivity to anesthesia. Moreover, it is really undesirable for children with muscle weakness to anesthetize. The conchotome percutaneous muscle biopsy is performed under local anesthesia in combination with Midazolam. Besides the replacement of general anesthesia by giving Midazolam, the diagnostic process will be accelerated introducing this method.

Should this study show that a conchotome percutaneous muscle biopsy is only valid for measuring energy production and not for substrate oxidation rates and enzyme complex activities, it is also possible to provide accessible screening for mitochondrial dysfunction in a larger group of patients. A open muscle biopsy will only be performed in those children who have a high suspicion, based on clinical symptoms or a combination of clinical symptoms with a decreased energy production in the conchotome percutaneous muscle biopsy. Hereby, fewer patients will be anesthetized unnecessarily.
Although there is currently no treatment for mitochondrial diseases, to find a diagnosis is of major importance for the child and the family. The clinical condition of the child can be managed by the improvement of nutrition, exercise and avoiding certain medications. For the family it is generally important to have a diagnosis because of psychological aspects and related to family planning. Moreover, in mitochondrial mutations that have an inheritance of theoretically 100%, other affected family members detected early and treated preventively. Also, the conchotome percutaneous muscle biopsy may be a good follow-up tool for future experimental treatments.

Study objective

Primary objective:
The validation of the conchotome percutaneous muscle biopsy to measure ATP production in patients suspected of mitochondrial disease.
Secondary objectives:
The validation of the conchotome percutaneous muscle biopsy to measure substrate oxidation rates and enzyme complex activity in patients suspected of a mitochondrial disorder.
Register the complications of conchotome percutaneous muscle biopsy.

Study design

This study will be conducted in phases. In the first phase, the diagnostic value of the method investigated (the correlation between the gold standard and the values found in the biopsy is done with the new method) in 10 patients. Thereafter, 30 additional patients will be added to this study to obtain reference values, in which the musculus vastus lateralis value (gold standard) is used as a reference for the new biopsy.

Patients suspected of a mitochondrial disease, planned for an open muscle

biopsy will be contacted for participating in this study.
After informed consent a piece of tissue be removed through the conchotome percutaneous muscle biopsy will be removed, in combination with the open muscle biopsy under general anesthesia.

The procedure of conchotome percutaneous muscle biopsy, as implemented in Sweden and England, is as follows:
- Midazolam Sedation by 0.3 mg / kg oral / rectal
- Pain relief by Paracetamol 20 mg / kg oral / rectal
- Local anesthesia using Lidocaine 2 cm around the site of incision
(To avoid injecting into the muscle)
- Incision (0,5 - 1 cm) of skin and fascia with a scalpel with a straight tip
- Collection of 40 mg of muscle with a nasal forceps (Karl Storz 456 001)
- Directly in sterile 0.9% NaCl on ice.
- Analysis within one hour of both samples.
- Wound pressure
- Close to Steris Breaks
- Delete Steris Breaks after 1 week
- No severe exercise for 24 hours and no bath for 1 week

In our study we will not give Midazolam since the children are already under anesthesia. The pain relief with acetaminophen is part of the protocol for open muscle biopsy. Local anesthesia will be applied as they can intervene with the confidence of the biopsy.

The conchotome percutaneous muscle biopsy will take about 10 minutes extra, since it probably not possible to perform it parallel with the open muscle biopsy.

The complications of the incision will be prosecuted by the responsible nurse.

The principal investigator will learn the technique of conchotome percutaneous muscle biopsies in Sweden. All conchotome percutaneous muscle biopsies will be performed by the principal investigator.

Study burden and risks

In this study we will acquire a piece of muscle under general anesthesia. Obviously this procedure has a risk on complications such as bleeding, infection and pain. Also there will be an additional scar from approximately 0,5 - 1 cm. It is known that complications of a open muscle biopsy are very rare, after the operation where a 4 cm incision is made. We therefore expect few complaints of this additional incision.
We consider the risk very small compared to the benefits which can be booked for the diagnostic procedure for mitochondrial diseases.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

- Age 0 - 18 years
- Approximately symmetrical use of both legs

Exclusion criteria

- Age > 18 years
- Assymatrical use of one leg, for example hemiparesis

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-03-2011
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	06-01-2011
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	NL33580.091.10