Prospective study into submicroscopic chromosomal abnormalities in foetuses with structural malformations on ultrasound

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Ethical review	Approved WMO
Status	Pending
Health condition type	Foetal complications
Study type	Observational invasive

Summary

ID

NL-OMON30792

Source
ToetsingOnline

Brief title
Submicroscopic chromosomal abnormalities and fetal malformations

Condition

- Foetal complications

Synonym
submicroscopic chromosomal abnormalities of the subtelomeres; small DNA defects

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: amniocentesis, microdeletion, MLPA, subtelomeres

Outcome measures

Primary outcome

The overall percentage of submicroscopic chromosomal abnormalities(

microdeletions or -duplications) in fetuses with structural malformations and a

normal routine karyotyping

Secondary outcome

1 Percentage of relevant submicroscopic chromosomal abnormalities

with known clinical implications versus the percentage of unknown abnormalities

with unclear clinical implications in fetuses with structural malformations and

normal routine karyotyping?

2. Can we ascertain an association between the fetal malformation and the

detected submicroscopic chromosomal abnormality?

Study description

Background summary

When a fetal structural abnormality is detected on ultrasound, amniocentesis or chorion villus sampling is often performed, in order to confirm or to exclude a chromosomal abnormality.
Firstly, a chromosomal abnormality could explain the ultrasound findings.
Secondly, a chromosomal abnormality could clarify the prognosis as often, chromosomal abnormalities are associated with mental retardation.

Only in a limited percentage of these cases, a chromosomal abnormality will be found with routine karyotyping. Therefore, it is possible that submicroscopic (microdeletions and - duplications) chromosomal abnormalities are involved that

could explain the malformation(s).

Study objective

The aim of this study is to investigate whether it is possible to improve genetic diagnostic testing in case of fetal abnormalities and a normal karyotype. We are interested in the relevance of the additional genetic testing. We wish to study the presence of submicroscopic (microdeletions and -duplications) chromosomal abnormalities using Multiplex Ligation Probe Amplification (MLPA), a molecular technique.

Study design

Prospective non-randomised or blinded study in fetuses with a malformation(s) on ultrasound for which the patient ahs already decided on karyotyping by amniocentesis.
In case the result of karyotyping is normal, MLPA will be used to detect submicroscopic chromosomal deletions of duplications, either at the ends of the chromosome (the subtelomeres) or elsewhere in the chromosome (interstitial) as it is known that genetic defects in these regions can cause severe syndromal abnormalities.

Study burden and risks

For this study, the same amount of amniotic fluid will be needed as for normal karyotyping (20- 22 cc).
Both parents will be asked to donate 10 cc of blood.
Tk
he risk of venous blood sampling is negligable.

Both parents need to sign an informed consent form as to give their permission for participation in the study as explained in the patient information letter.

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

Only if amniocentesis is already planned because of abnormal ultrasonographic findings of the fetus, future parents will be asked for this study.
The MLPA-test will only be performed if the karyotyping is normal.

Exclusion criteria

Abnormal fetal karyotype that can explain the ultrasonographic anomalies.
Absence of a signed informed consent by both parents.

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):	01-04-2007
Enrollment:	130
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	NL16106.091.07