European Non-invasive Trisomy Evaluation (EU-NITE Study): Evaluation of a targeted analysis of cell free fetal DNA in maternal blood for prenatal diagnosis of fetal trisomies.

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our primary aim is to validate a targeted analysis of circulating DNA in maternal blood by assessing the diagnostic accuracy for fetal trisomy 21. In addition, test characteristics for fetal trisomy 18 detection will be evaluated.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON36065

Source
ToetsingOnline

Brief title
EU-NITE

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
chromosomal aberration, trisomy

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Tandem Diagnostics, San Jose CA 95138. USA

Intervention

Keyword: detection, fetal DNA, maternal blood

Outcome measures

Primary outcome

detection rate of trisomies with Tandem SNPs

Secondary outcome

not applicable

Study description

Background summary

Since the 1970s, pregnant women are offered prenatal screening or prenatal diagnostic testing for Down*s syndrome. The standard diagnostic test, karyotyping on cultured fetal or placental cells, also reveals, if present, other chromosomal aberrations such as trisomy 18, 13 or sex chromosome anomalies. The main aim to test for genetic diseases is to provide reassurance to parents with an increased risk of an abnormal fetus, and for the minority who receives an unfavourable outcome, to provide the option of terminating the pregnancy. This option is chosen by more than 90% of parents when confronted with the diagnosis of Down*s syndrome.
To check for fetal chromosomal aberrations, fetal cells can be acquired by chorionic villus sampling or amniocentesis. Traditionally, microscopic visual assessment of the shape and number of the fetal chromosomes, called karyotyping is then performed. This assessment is only possible in dividing cells, which means that a chromosome culture is necessary. Because of this culture time, it can take up to 14-21 days before a reliable test result can be reported to the patient. The currently available tests, chorionic villus sampling and amniocentesis, are highly reliable with practically 100% sensitivity and specificity for the detection of fetal trisomies. The main disadvantage however is the invasive nature of the diagnostic tests. Both tests are associated with a procedure-related fetal loss rate of 0.5-1%.

Recently real-time polymerase chain reaction (PCR) techniques have allowed the identification and quantification of fetal DNA in the maternal blood. Fetal sex determination with Y-chromosome-PCR and Rhesus-D typing has been found to have a specificity of 100% and a sensitivity of 96%. Both of these diagnostic tests have important clinical applications, for X-linked genetic disorders and Rh-disease respectively, and have already been implemented in clinical care. However, these tests rely on the absence of a copy gene in the mother, and are not suitable for trisomy detection.

Recently, new approaches have been introduced aimed at detection of fetal trisomies (and potentially many other genetic diseases) using a maternal blood sample. Some methods utilize a targeted analysis of circulating DNA in maternal blood. In one pilot study whereby tandem SNPs were used for the targeted analysis, the accuracy of trisomy 21 detection was 100%.

Study objective

our primary aim is to validate a targeted analysis of circulating DNA in maternal blood by assessing the diagnostic accuracy for fetal trisomy 21. In addition, test characteristics for fetal trisomy 18 detection will be evaluated.

Study design

In a prospective, consecutive cohort of pregnant women scheduled to undergo invasive diagnostic testing, a blood sample will be taken prior to invasive procedure.

Study burden and risks

venous puncture

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

Singleton pregnancy with gestational age between 9 and 23 weeks, informed consent.

Exclusion criteria

Invasive procedure performed prior to taking the blood sample, history or active significant malignancy in the mother requiring major surgery or systemic chemotherapy, language restriction with failure to understand the study information.

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):	01-06-2011
Enrollment:	630
Type:	Actual

Ethics review

Approved WMO Date:	27-05-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-02-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL35941.058.11