Non- invasive prenatal diagnosis using cell-free fetal DNA (cffDNA) in maternal plasma

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Developing a non-invasive test for detection of trisomy 21,13 orr 18 in the unborn fetusDeveloping a standardised protocol, inclusive quality criteria for the use of massive parallel sequencing of celfree fetal DNA in maternal plasmaOptimalising...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and hereditary disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON36898

Source
ToetsingOnline

Brief title
NIPD

Condition

- Congenital and hereditary disorders NEC
- Foetal complications

Synonym
congenital anomalies, down syndrome

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cell free fetal DNA in maternal plasma, Prenatal Diagnosis

Outcome measures

Primary outcome

Feasability of non-invasive foetal aneuploidy testing in the UMCU, technical performance, technical failures, throughput, turnaround time and costs, sensitivity in a high risk population

Secondary outcome

-Critical parameters influencing the amount of foetal DNA in the maternal plasma such as maternal weight, gestational age and obstetric complications

Study description

Background summary

Invasive prenatal diagnosis for chromosome anomalies is being offered to all women with an elevated risk. If chosen by the pregnant woman and her partner it is perfomed with chorionic villus sampling or amniocentesis. These tests entail a small but unavoidable risk of iatrogenic pregnancy loss of ca 0,5 %. In the Netherlands invasive prenatal diagnosis is performed 8000 times on an annual base. Non-invasive diagnosis of monogenic conditions inherited from the father has been possible since 1997 and has been used amongst others by ourselves in fetal sexing for medical reasons and fetal Rh D blood group typing. Since 2011 the introduction of massive parallel sequencing has made it possible to quantify cell free fetal DNA in maternal plasma and link it to its chromosomal origin. This has opened the possibility for fetal Down syndrome detection in maternal plasma. The test is now being offered in patient care in a number of centers abroad. The published sensitivity for trisomy 21 is high (100 % with a CI 95.9-100). the percentage false positive results is 1 %, substantially lower than the currently used combination test (5 %). In the Netherlands a multidisciplinary consortium called NITRO (www.nipdnederland.nl) is active. Amongst others geneticists, gynaecologists, laboratory specialists in clinical genetics and ethicists of all academic centres participate as well as the National Institute of Public Health (RIVM). The aim of the consortium is to introduce NIPD in the Netherlands. A first step is that each

participating centre gets expertise in performing the test with the locally available equipment and platforms, and gives testimony of its ability to do so according to the standards.

Study objective

Developing a non-invasive test for detection of trisomy 21,13 orr 18 in the unborn fetus
Developing a standardised protocol, inclusive quality criteria for the use of massive parallel sequencing of celfree fetal DNA in maternal plasma
Optimalising throughput, turnaround time and costs

Study design

In order to achieve the study objectives we require plasma and DNA fractions of women with and without a foetus with trisomy 21,13 or 18 in utero. For this purpose we will collect blood from women who report for invasive prenatal diagnosis and who request foetal karyotyping. These women have a higher than average risk for a foetus with one of these trisomies. Blood will be sampled before the invasive procedure. After blood sampling the material will be transported asap to the labs of the Department Medical Genetics UMCU. Cells will be separated from plasma according to already validated procedures. Plasma will be stored. From samples where the foetus appears to have a trisomy according to the analysis of chorionic villi or amniotic fluid, cffDNA will be extracted. The same will be done for a number of samples where the foetus has a normal karyotype. Fetal DNA analysis will be done using the platforms available in the laboratories of the Department of Medical Genetics.

Study burden and risks

Risks and burden associated with venapunction. One venapunction will be done, preceding the invasive procedure. No extra hospital or lab visits will be required. The amount of blood taken (20 ml) is comparable to the amount taken for normal diagnostic procedures during pregnancy. Participation in the project does not reveal additional information, and the patient will not be informed of the results of the blood test.
The patient will be requested to send us a follow up form at the end of pregnancy. She will be given a standard form and prestamped envelope for this purpose This is already a standard procedure, part of our normal care evaluation process. Finally she will be asked if she agrees us asking additonal information on the outcome of pregnancy from her caregiver, if necessary to evaluate the effect of pregnancy complications on the amount of ffDNA in maternal plasma in case of outliners. Risks and burden are hence minimal.

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

Pregnant women who have chosen for an invasive prenatal diagnostic test
Vital pregnancy

Exclusion criteria

patient is unable to understand information and give informede consent e.g. due to language barrier;
pregnant woman with chromosome anomaly;
age younger than 18 yrs

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):	01-10-2012
Enrollment:	2250
Type:	Actual

Ethics review

Approved WMO

Date:	31-08-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL41009.041.12