Non-invasive diagnosis of fetal Down syndrome using fetal DNA or RNA present in the maternal blood

Published: 24-03-2009
Last updated: 05-05-2024

The final aim of the study is the implementation of a test for the detection of fetal Down syndrome via noninvasive procedures, with the same characteristics as the tests that are currently being used (sensitivity and specificity). This test can...

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

Summary

ID

NL-OMON32725

Source
ToetsingOnline

Brief title
Non-invasive diagnosis of fetal Down syndrome

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Neonatal and perinatal conditions

Synonym
Down syndrome, trisomy 21

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: Down syndrome, maternal blood, non-invasive diagnosis

Outcome measures

Primary outcome

As the test is suppose to replace the current non-invasive and invasive tests (for specific referral reasons), the characteristics of the test will have to be comparable to the current tests, as far as sensitivity and specificity are concerned.

Secondary outcome

Besides sensitivity and specificity, the robustness of the test has to be studied too (the number of technical failures).

As far as is known now, blood samples will have to be processed soon after withdrawal. A routine diagnostic test might be hampered by this, as not all samples will be drawn in the institute in which the test is performed and they may not always reach the laboratory within limited time (e.g. due to trafic). Therefore, before implementation into routine diagnosis, logistics will have to be studied (end of phase 2).

Study description

Background summary

To study the presence or absence of fetal Down syndrome, invasive diagnostic procedures, such as amniocenteses or chorionic villus biopsy, are necessary. Such procedures carry a risk of pregnancy loss, which is estimated to be 0.3-0.5%. Well-defined inclusion criteria are therefore needed to avoid

unnecessary procedure-related risks. Using noninvasive methods, such as examination of several factors in the maternal blood in combination with ultrasound scanning, only a risk of carrying a child with Down syndrome can be established, not a certainty.

For more than 15 years now researchers have explored the use of fetal cells, DNA or RNA in the maternal blood for fetal Down syndrome detection. Recently, important progress has been made by the group of prod dr Lo from Hong Kong, as they described a method with which the presence or absence of fetal Down syndrome can be established using maternal blood only, i.e. without an invasive procedure. Worldwide, several groups are working on this challenging field, leader in this being the American company Sequenom. Together with the grop of Dennis Lo, they further developed a test, which is now being validated. So far, the results are informative in 95% of the US population, and for those pregnant women for whom it can be used, the sensitivity and specificity for the detection of fetal Down syndrome is 100%.

Study objective

The final aim of the study is the implementation of a test for the detection of fetal Down syndrome via noninvasive procedures, with the same characteristics as the tests that are currently being used (sensitivity and specificity). This test can then replace the present combination of noninvasive screening followed by an invasive diagnostic test. As worldwide much effort is put into the development of such a test, we expect a test becoming commercially available in 2009. Thus, the aim of the present study is not the development of such a test, but the validation of it once a test has become available.

Therefore, a study has to be conducted which can be divided into three phases:
Phase 1: in this phase, there is no commercially available test. Only blood from pregnant women will be collected and stored in such a way that, once a test becomes available, they can be used to validate the test in our own laboratory. Phase 2: a test is commercially available. In this phase the test will be validated on our own lab with the materials that we collected in phase 1. Furthermore, collection of material will continu during phase 2.
Phase 3: this phase will only follow when the test has proven to be potentially suitable for diagnostic use. In this phase, the test will be performed on large numbers of samples, collected in all centres of the Nijmegen Network of Prenatal Diagnosis.

The present project only concerns phases 1 and 2.

Study design

As mentioned above, in phase 1, blood of pregnant women will be collected and stored in such a way that fetal DNA / RNA can be isolated from it and tested,

once the test becomes available (phase 2, estimation: second part of 2009).

Study burden and risks

The risk of venous blood sampling is negligable.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Postbus 9101
6500 HB Nijmegen
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Postbus 9101
6500 HB Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Only if an invasive procedure is planned, pregnant women will be asked to participate in the study. Main focus will be pregant women in the first trimester of pregnancy. However, to validate the methods to be used, also a small group of pregnant women with other gestational ages will be asked to participate as well as pregnant women who already

underwent an invasive test. Furthermore, a small control group of man and non-pregnant women will be asked to participate.

Exclusion criteria

After the initial phase, during which the methods to be used have to be validated and during which pregnant women who already underwent an invasive test and/or with an gestational age of more than 12 weeks can be included, women who already underwent an invasive test will be excluded.
Furthermore, samples will not be included if informed consent is not signed.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-03-2010
Enrollment:	260
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	24-03-2009
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	NL25347.091.08