Consequences and Risk factors Of congenital CytomegalovirUS infection

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- To assess the burden of disease of congenital CMV infection in the Netherlands at the age of 5 to 6 years through the assessment of the occurrence of sensorineural hearing loss due to congenital CMV infection.- To establish the burden of disease...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON39637

Source
ToetsingOnline

Brief title
CROCUS-study

Condition

- Neurological disorders congenital
- Viral infectious disorders
- Congenital and peripartum neurological conditions

Synonym
congenital CMV infection, congenital cytomegalovirus infection

Research involving
Human

Sponsors and support

Primary sponsor: RIVM
Source(s) of monetary or material Support: Strategisch Onderzoek RIVM (SOR)

Intervention

Keyword: Congenital cytomegalovirus infection, Disease burden

Outcome measures

Primary outcome

Hearing function at the age of 5 to 6 years

Secondary outcome

- Neonatal hearing function and cognitive function, motor function, visual

function and growth during childhood (0 to 6 years)

- Quality of life of the children (at the age of 5 to 6 years) and of their

parents.

- Viral load of CMV in the dried blood spots.

Additional study:

- Predictive factors for the outcome of congenital CMV infection.

Study description

Background summary

Cytomegalovirus (CMV) is a member of the herpes virus family with the capacity of lifelong latency and intermittent reactivation. CMV infection is common among the general population. In the USA, between 1988 and 1994, 58% of the women of childbearing age was IgG-seropositive, indicating previous CMV-infection. The overall seroprevalence for CMV infection in the Netherlands in 2006-2007 was 49%. In healthy individuals it rarely causes symptoms. In contrast, fetal infection with CMV can cause significant morbidity.
Congenital CMV infection can occur with a primary maternal CMV-infection or with a recurrent maternal CMV-infection (re-infection or reactivation).
In the Netherlands the birth prevalence of congenital CMV infection in 2007 was estimated at 0.5%, which is in accordance with the reported world-wide prevalence of 0.6-0.7%.

International studies have shown that congenital CMV infection can cause severe disability in young children. About 10 to 15% of children with congenital CMV infection show symptoms at birth. The typical symptoms at birth include blue-berry muffin rash, petechiae, microcephaly, low birth weight, hepatosplenomegaly and jaundice. Of these children approximately half will develop long term sequelae such as sensorineural hearing loss, visual impairment and mental retardation. Notably of the almost 90% of children with initial asymptomatic congenital CMV infection, 10-15% may develop long term sequelae, predominantly hearing loss.
Insight into the disease burden due to congenital CMV infections including long term sequelae in the Netherlands is lacking. With the aim to prevent serious consequences of congenital CMV infection in the future, this insight is needed to be able to estimate the population impact of primary and secondary prevention measures.

Study objective

- To assess the burden of disease of congenital CMV infection in the Netherlands at the age of 5 to 6 years through the assessment of the occurrence of sensorineural hearing loss due to congenital CMV infection.
- To establish the burden of disease of congenital CMV infection in the Netherlands during early childhood (0-6 year) through retrospective evaluation of the reported long-term sequelae of congenital CMV infection, including neonatal hearing loss and visual, cognitive and motor impairment and through the evaluation of the quality of life of both children and their parents.
- To determine the association between CMV viral load in dried blood spots and long-term sequelae of congenital CMV infection.

This study enables the assessment of the disease burden of congenital CMV infection in the Netherlands at the age of 5 to 6 years. Many international studies describing the burden of disease had a short follow-up term (up to 3 years). The added value of the proposed study is that insight will be given in the long term consequences of congenital CMV infection and the specific situation in the Netherlands. This information is essential to assess both the need and the potential benefits of primary and secondary preventive measures that are expected in the future.

Study design

For this study we will test, with consent of the parents, around 25.000 dried blood spots (DBS) for congenital CMV infection. We expect to find about 135 children with congenital CMV infection. We intend to include at least 100 children with congenital CMV infection and at least 200 children without congenital CMV infection. Of these children we will request information that is routinely collected during regular examinations by the youth health care organization. We will request data from the preventive health check at the age

of 5 or 6 years and the schoolresults of the first two years in primary school. In addition we will ask parents to fill out for questionnaires. One concerning the health of their child and demographic features of their family, one on the development of their child and two short questionnaires to assess the quality of life of both the children and their parents. Finally we will request data from the child health centre visits and the neonatal hearing screening.

Study burden and risks

The burden of this observational study is minimal for the children and their parents. There are no apparent risks involved in this study.
Congenital CMV infection will be assessed retrospectively in dried blood spots which have been collected almost 5 years previously. Therefore no blood sample has to be taken from the child for the diagnosis of congenital CMV infection.
The clinical outcome measures will be predominantly assessed during the child health centre visits and the voluntary standard preventive health check by the youth health care organization. These assessments routinely take place and are independent of participation in the study.
In addition to the standard youth health care examinations the parents will be asked to fill out for questionnaires.A general questionnaire, concerning demographic features of the child and parents, a questionnaire concerning the development of their child (Child Development Inventory, CDI) and two questionnaires concerning the quality of life of both the children and their parents. This will take approximately two to two and a half hours of their time in total.
However the knowledge that the child has congenital CMV infection, even if the child will never develop sequelae, can have impact on parents since they might be anxious about the possible consequences of this congenital infection.

For the children in the study the assessment of CMV in DBS will allow the retrospective diagnosis of congenital CMV infection. This will lead to a possible explanation for potential disabilities of the child that are detected during or before this study.
The knowledge of the underlying reason of the disabilities of their child can be a relief for parents. Disabilities can affect parents and families on emotional, practical and psychological level and a clarification of the possible cause of disabilities can sometimes enhance the coping with these difficulties.
On a broader level this study will provide knowledge on the burden of disease in congenital CMV infection at the age of 5 to 6 years and its risk factors. It will contribute to the considerations with regard to primary and secondary preventive measures. For example with the introduction of neonatal screening for congenital CMV infection an additional hearing screening between the age of 1 to 5 years could be establish for children who are at risk for hearing loss. This would enable early recognition and intervention which could improve the development of the child.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Children who underwent neonatal screening and of whom the dried blood spot is stored for 5 years. (Phase 1, n <= 25.000)
- Children with a congenital CMV infection and a twice as large control group without congenital CMV infection as detected by PCR (polymerase chain reaction) analysis of the dried blood spot. (Phase 2, n <= 300)

Exclusion criteria

- Children who did not participate in neonatal screening
- Chidren whose dried blood spots are not stored for 5 years
- No informed consent of parents for testing the dried blood spots or participation in the study

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-10-2012
Enrollment:	25000
Type:	Actual

Ethics review

Approved WMO Date:	25-07-2012
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-09-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	08-11-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-03-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Approved WMO Date:	21-08-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	01-08-2014
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

ID: 22019
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL39787.058.12
OMON	NL-OMON22019