Markers for neurocognitive impairment in congenitally CMV infected infants: MARVELYS study

Published: 19-04-2016
Last updated: 19-04-2024

1. To characterize long-term neurologic- and cognitive disorders, audiological and ophthalmological alterations in cCMV-infected children.2. To identify immunological, neurological host factors and virological factors that are predictive of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON43495

Source
ToetsingOnline

Brief title
MARVELYS study

Condition

- Skin and subcutaneous tissue disorders NEC
- Viral infectious disorders
- Central nervous system infections and inflammations

Synonym
congenital cytomegalovirus infection

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

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

Intervention

Keyword: children, congenital CMV infection, long term outcomes, prognostic factors

Outcome measures

Primary outcome

Main endpoints are neurocognitive performance, deviations in neuroimaging parameters, audiological and ophthalmological measurements at the age of one, two, five and eight years of age. CSF and blood parameters will be measured and correlated to the results of the above mentioned tests.

We expect to find various immunological, neurological host factors and virological factors predictive of poor neurological and cognitive outcome in our study group.

The results of this study may have direct implications for the direct patient care of these children, as they may need timely alterations in medical treatment and/or referral for supportive therapy.

Secondary outcome

not applicable

Study description

Background summary

Rationale: Congenital cytomegalovirus (cCMV) infection is the leading cause of congenital viral infection worldwide and can cause serious disease to the newborn. In 15%-23% of CMV infected neonates signs of symptomatic disease are present at birth, such as intrauterine growth restriction, hepatosplenomegaly or microcephaly. Of these symptomatic children, 90% will develop additional complications within the first two years of life. The most important long-term

complications are due to central nervous system (CNS) damage, of which hearing and visual impairment and mental retardation are the most common. In case of cCMV infection without symptoms at birth, 10- 15% of the affected children will develop one or more long-term neurological sequelae.
The exact prevalence of congenital CMV infection in the Netherlands is not known, but recent estimates calculated a prevalence rate at 0.54% (de Vries, 2011), leading to annual incidence of 1000 children are born with cCMV infection in the Netherlands, of whom at least 180 children (0.1% of all newborns) will be affected by long term neurologic sequelae.
Currently there is no prenatal intervention to prevent CMV transmission from mother to child and thus prevent or reduce neonatal neurologic damage. Postnatal antiviral treatment with (val)ganciclovir is the state-of-the art treatment of symptomatic cCMV disease. The outcome of cCMV infected children varies significantly and prognostic predictors of outcome in CMV infected children are missing. To understand the pathogenesis of neurological and neurocognitive deficits in cCMV infected patients, long term evaluation starting at the earliest age possible is necessary. Immunological and neurological host factors, as well as virological and pharmacological factors most likely play a role in the outcomes of cCMV infected children. We hypothesize that the several immunological, neurological host factors and virological and pharmacological factors may influence long term outcomes of cCMV infected children.

Study objective

1. To characterize long-term neurologic- and cognitive disorders, audiological and ophthalmological alterations in cCMV-infected children.
2. To identify immunological, neurological host factors and virological factors that are predictive of neurological and neurocognitive impairments in cCMV infected infants.
3. To evaluate the added value of advanced Magnetic Resonance Imaging (MRI) techniques, including Diffusion Tensor Imaging (DTI), Magnetic Resonance Spectroscopy (MRS) and Arterial Spin Labelling (ASL) to predict neurological outcome within this pediatric population.

Study design

prospective longitudinal observational study

Study burden and risks

This study is classified as an observational study in subjects incompetent to give informed consent. CCMV infected infants will undergo as part of their standard treatment plan neuropsychological assessments (NPA), MRI neuroimaging, audiological and ophthalmological examination. As part of their standard treatment plan, cCMV infected children will undergo venous blood sampling at

various time points in the follow up period according to international and AMC guidelines. Extra blood samples to evaluate immunological and neurological host factors will be collected during routine vena punctures (VP) that are performed as standard patient care (6,5 ml of blood taken at 7 time point during 8 years). For this study, the study participant will undergo a novel neuro-imaging using novel MRI technique (3Tesla) instead of the conventional 1,5 Tesla MRI imaging. For this study, the study participant will undergo an NPA, MRI neuroimaging, audiological and ophthalmological examination at the age of eight years. At the age of eight year, the study participants will undergo a venous blood draw and sampling. Children younger than three months of age and older than eight years of age can undergo MRI imaging without general anesthesia.
All parents and/or caregivers of the study participants will be given extensive information on all the tests that need to be taken as part of routine patient care as well as part of this study. Patients will be included on voluntary basis. During all procedures we will guarantee guidance from research staff for all participants. Parents/guardians can join their child at all times.
CCMV infants may later develop sequelae. To understand the pathogenesis of neurological and neurocognitive deficits in these patients long term evaluation starting at the earliest age possible is necessary. Therefore we aim to include neonates with a cCMV infection as early as possible in life to be able to tailor medical treatment and initiate supportive care if needed as soon as possible.
We expect to find various prognostic (host) factors of poor neurological and cognitive outcome in our study group. Former comparable pediatric neuro-imaging and NPA studies have obtained medical ethical approval and have produced satisfying results (Cohen CID 2015, Cohen Neurology 2015, Aukema,2009).

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 5
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 5
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

•Positive Polymerase Chain Reaction (PCR) detection of the CMV in urine or blood in neonates younger than 10 days of life and/or positive CMV PCR in dried blood spot (Guthriecard) in children older than 10 days of age
•Age: birth - three months of age
•Written informed consent from the parent(s) or guardian(s).

Exclusion criteria

•No signed consent from the parent(s) or guardian(s).
•MRI contra-indications (e.g. implanted active devices such as pacemakers or medication pumps)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-05-2016
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	19-04-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL55672.018.15