Role of neutralizing (maternal) antibodies in protection against human parechovirus infection and other risk factors for picornavirus infection in young children.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON33777

Source
ToetsingOnline

Brief title
Role of antibodies in human parechovirus infection in young children.

Condition

- Viral infectious disorders

Synonym
infection with human parechovirus, meningitis/sepsis like illness

Research involving
Human

Sponsors and support

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

Intervention

Keyword: (maternal) antibodies, human parechovirus infection, risk factors, young children

Outcome measures

Primary outcome

- HPeV specific antibodytiters

- Severity of disease

Secondary outcome

- Cytokine production

- Genetic variables: CTLA-4 polymorphism and expression of Toll Like Receptors

- Duration of shedding of HPeV

- Viral load of HPeV

Study description

Background summary

EV infections are generally recognized as among the most common causes of sepsis or meningitis in young children. The clinical importance of HPeV infection in young children and especially neonates is increasingly recognized. In some children the morbidity is considerable with sepsis-like illness or/and meningitis and possible long term sequelae. However, no effective treatment is known. Since lack of type-specific antibodies in neonates is a risk factor for symptomatic neonatal EV infection, Intravenous immunglobuline (IVIg) is sometimes given in severe neonatal sepsis, but results are inconclusive. This could be due to differences in the circulating strains causing (severe) morbidity, and the antibodies present in IVIg against EV strains that have been circulating in the past. However, the protective role of antibodies against EV/HPeV infections has never been proven. The occurrence of over 100 EV serotypes with a large diversity of clinical syndromes makes it difficult to

study this group of viruses. The new group of HPeVs only contains six genotypes, with a distinct difference in severity of disease between HPeV1 and HPeV3, the most prevalent genotypes. Furthermore, the seroprevalence in adults of HPeV1 and 3 antibodies is much higher than for the EV serotypes. This differences, combined with their clinical and biological resemblance to the EVs, makes HPeV infection a suitable model for studying picornavirus pathogenesis.

Study objective

The aim of this study is to determine the risk factors in infants for obtaining a severe HPeV infection. For this purpose, we will test the hypothesis that (maternal) HPeV specific antibodies are protective against (severe) HPeV infections in young children. This will support, or reject, the rationale for antibody therapy in HPeV infection.
Furthermore, we will study the importance of viral and host factors in pathogenesis of picornavirus infections. Next to the presence or absence of maternal antibodies, viral load, virus tropism, or genetic host factors like polymorphisms or production of cytokines could influence severity of disease.

Study design

A case-control study of mother and child pairs to evaluate the role of maternal antibodies against HPeV-infection in young children and to determine other risk factors.
The cases are defined as HPeV positive and the controls are defined as HPeV negative and either EV positive or also EV negative.

Study burden and risks

For this study a single blood sample will be obtained from the infants and their mothers. If possible, this sample will be obtained together with necessary blood samples for treatment. Untill now, no serious adverse reactions are known from a single venous punction.
A stool sample is also obtained for diagnostics of HPeV ad EV infection. Additional stool samples of HPeV positive infants will be obtained every two weeks, until HPeV is negative.
The aim of this study is to determine the role of (maternal) antibodies. If these antibodies are protective, they possibly can be used as medicine for this serious infection in the future .
We think this possible benefit for the future outweight the risks for participating in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Infants under the age of 1 year, positive for HPeV in CSF, stool, nasopharynx and/or blood obtained for diagnostic purposes and detected by routine PCR.
Controls under the age of 1 year will be randomly selected from the diagnostic CSF, stool, nasopharynx and/or blood samples positive for EV PCR and negative for EV/HPeV PCR, and matched for age.
The mothers of those infants.
Written informed consent.

Exclusion criteria

No informed consent

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-05-2009
Enrollment:	216
Type:	Actual

Ethics review

Approved WMO

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	NL26242.018.09