Neurological, visual and neurocognitive performance in pediatric HIV-1- infected patients as compared to healthy controls.

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To evaluate neurologic- and cognitive disorders, neuroimaging and ophthalmological alterations in perinatally HIV-infected children in comparison to matched (with respect to age, sex, race, home environment and socio-economic status) healthy…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON37553

Source
ToetsingOnline

Brief title
NOVICE

Condition

- Immunodeficiency syndromes
- Viral infectious disorders
- Central nervous system infections and inflammations

Synonym
brain disease, neurologic and neuropsychologic impairment

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Stichting tot Steun Emma Kinderziekenhuis,Abbott

Intervention

Keyword: Children, HIV, Neurology

Outcome measures

Primary outcome

Main endpoints are diminished neurocognitive performance, deviations in neuroimaging parameters and ophthalmological measurements, comparing HIV positive cases to healthy controls. Several CSF and blood parameters will be measured and correlated to the results of the above mentioned tests.

Secondary outcome

nvt

Study description

Background summary

Before the era of combined antiretroviral therapy (cART), perinatally infected HIV-positive children frequently presented with serious neurological dysfunctioning (prevalence varying from 30%-50%), including HIV-encephalopathy, as characterized by impaired brain growth and acquired microcephaly, symmetrical motor deficits and loss of or failure to attain developmental milestones. Early neuroimaging studies of HIV-encephalopathy using computed tomography (CT) demonstrated cerebral atrophy, calcifications in the basal ganglia and white matter changes2. Since HIV-infected children are being treated with cART, the incidence of HIV-encephalopathy has decreased while in the meantime neuro-imaging abnormalities shown by these conventional neuroimaging techniques have improved. Children can present with other neurologic disorders such as seizures, headaches and neurocognitive impairments (e.g. learning-, behavioural-, and motor deficits). The etiology of this neurocognitive impairment is complex and, most likely, not purely biologically

determined. Environmental factors, such as home environment and socioeconomic status (SES), may play a confounding role in cognitive development. In our patient group, the SES is generally lower than in the average population. Comparative data on neurological and neurocognitive findings between HIV-infected and healthy controls with equal SES and living within similar environments are lacking.
Since neurological and neurocognitive disorders can not be diagnosed until they are clinically obvious, the availability of objective, reliable, non-invasive markers may offer great advantages in assessing early central nervous system (CNS) involvement in HIV-positive children. Standardized neuropsychological assessment (NPA) and several advanced neuroimaging tests as well as ophthalmological measurements are available to study the neurological, neurocognitive and ophthalmological disorders in HIV-positive children. In addition, biochemical tests and measurement of cART concentration levels in cerebrospinal fluid (CSF) and blood, and combining these results with the earlier mentioned NPA, neuroimaging and ophthalmological tests, will provide more insight in the pathophysiology of CNS involvement of HIV and its clinical consequences.

Study objective

To evaluate neurologic- and cognitive disorders, neuroimaging and ophthalmological alterations in perinatally HIV-infected children in comparison to matched (with respect to age, sex, race, home environment and socio-economic status) healthy controls. To measure cART concentration levels in CSF and blood and correlating the results with the outcome of the NPA, neuroimaging and ophthalmological tests.

Study design

An observational cross-sectional case-control study in which all participants will undergo neuropsychological tests (NPA), advanced MRI techniques (MRS, DTI, ASL), and ophthalmological investigation (optical coherence tomography; OCT). In addition, several clinical and laboratory factors will be measured.

Study burden and risks

This study is classified as an observational study in subjects incompetent to give informed consent. HIV positive children will undergo NPA, MRI, LP and venous blood sampling as part of their normal treatment plan. For this study, they will undergo one additional MRI and LP, and one ophthalmological examination. Any venous blood sampling will as much as possible be combined with standard blood sampling.
Controls are previously unexposed to any of the examinations. All patients are given extensive information on all tests and 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 except the NPA, which will be taken by an experienced pediatric neuropsychologist will guide the participant.
Our research question is group related. To understand the pathophysiology of neurocognitive deficits still found in HIV positive children (in the era of cART) we need to evaluate patients at an age as early as possible, without the confounding factors of general aging. We need the control group to minimize confounding effects of sex, age, race, home environment and socioeconomic status.
By accomplishing this study, we may be able to diagnose neurological and neurocognitive disorders at an early stage in HIV positive patients. The patients may benefit from close monitoring, and in the future early intervention could improve their general development.
Former case-controlled pediatric neuro-imaging studies have obtained medical ethical approval and have produced satisfying results.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Cases: Perinatally infected with HIV
Cases/controls: 8-17 years of age

Exclusion criteria

Intracranial malignancy, history of traumatic brain injury with loss of consciousness > 30 minutes
Severe psychiatric disorders
MRI contra-indications (e.g. implanted active devices such as pacemakers or medication pumps, or metal splinters in eye, brain or lungs, claustrophobia)

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):	28-12-2012
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	02-08-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2013
Application type:	Amendment
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	NL40269.018.12