HIV-1 infection in infants and the unidentified susceptibility of white blood cells for retroviral infection

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The general objective of this study is to elucidate the cellular components for HIV-1 infection in children.

Ethical review	Approved WMO
Status	Pending
Health condition type	Immune disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON30327

Source
ToetsingOnline

Brief title
HIV-1 infection in infants

Condition

- Immune disorders NEC
- Viral infectious disorders

Synonym
AIDS, HIV-1-infection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cytokines, HIV-1, infants, lymphocytes

Outcome measures

Primary outcome

1. CCR5, other chemokine receptor and phenotype expression on cells derived from cord blood of healthy neonates and cord blood from neonates born to HIV-1-infected mothers.

2. define chemokine receptor upregulation as well as phenotype alterations in cells from cord blood by proliferative stimulation via a.o. cytokines (e.g. IL-2, IL-7).

3. determine productive HIV-1 infection rates in vitro of naïve T cells and other white blood cells derived from cord blood of healthy neonates and cord blood from neonates born to HIV-1-infected mothers.

4. Test whether infection (3.) can be inhibited by CCR5 antagonists and monoclonal antibodies against other chemokines receptors.

5. rate of infection of the above cells isolated from the two sets of cord blood with HIV-1 strains obtained from HIV-1 infected children.

6. assess the repertoire of co-receptors for HIV-1 infection on CD4+ T cells and other white blood cells from young patients, i.e. CCR5, CCR2 and CXCR4 expression in the perspective of extensive subset definition of T cells (memory / naïve etc)

7. define the genomic form of HIV-1 in the subsequent white blood cells of HIV-infected infants, e.g. comparing the form of HIV-1 in naïve, memory T cell

subsets as well as blood monocytes.

Secondary outcome

nvt

Study description

Background summary

HIV-1 is still spreading rapidly, in particular in young women of childbearing age. This implies that children are at risk to become infected through maternal to child transmission (MTCT) of HIV-1 e.g. during pregnancy and delivery. Interventions to prevent transmission MTCT such as HAART and neonatal ART prophylaxis have reduced transmission from 25%-40% to less than 1 %. However there are reports suggesting long term effects of ART exposure regarding hematological and mitochondrial abnormalities. Thus current prevention strategies are successful but not ideal. Furthermore the number of HIV-1 infected children is also increasing. At the moment UNAIDS has estimated that approximately 2.300.000 children are infected with HIV-1. Thus the development of appropriate and successful treatment regimes for HIV-1 infected children are very important. A thorough understanding of the mechanisms involved in HIV-1-infection in children is mandatory to develop new successful strategies to prevent MTCT of HIV-1 and to increase success rates in the treatment of HIV-1 infected children. With this study we try to elucidate mechanisms during early HIV-1 infection in neonates.
The immune system in the newborn is immature, as the lymphocytes have not yet encountered micro-organisms. This is reflected by the presence of non-activated naïve T-cells (CD45RA+ CD27+ CCR7+). Encounter of these cells with the cognate antigen results in a maturation of the immune system with memory T cells (CD45RO+ CD27+ CCR7-).
HIV-1 is a virus that attacks the immune system by infecting predominantly CD4+ T cells. The virus binds to CD4 and co-receptors on the surface membrane of CD4+ T cells to enter the cell. Under normal conditions, the obligatory co-receptor for early HIV-1 entry, i.e. chemokine receptor CCR5, is not expressed on naive CD4+ T cells present in the neonate. However, neonates or even a fetus with hardly if any memory CD4+ T cells can become infected with HIV-1 through maternal-to-child-transmission (MTCT). HIV-1 infection in neonates also progresses more rapidly than in adults with higher plasma viral loads. Thus, although low if any numbers of CCR5+ T cells are present, rapid infection and replication of HIV-1 does occur in newly infected neonates and infants. The aim of this project is to resolve this paradox.

Study objective

The general objective of this study is to elucidate the cellular components for HIV-1 infection in children.

Study design

Prospective case *control study. Comparison of immunological parameters in 20 cord blood samples of children born to HIV-1-infected mothers and 20 cord blood samples of children born to healthy mothers.

Study burden and risks

The cord blood samples of the children born to HIV infected mothers are not an added burden, because a cord blood sample is always obtained for (a.o. the antiretroviral drug concentration in the cord blood) the current treatment protocol for prevention of mother to child transmission of HIV-1.
For the mother and child of the healthy mother it is an extra procedure during the delivery, however it does not need to interfere with the delivery. The risks for the new-born are absent

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy subjects: healthy pregnant women and their newborn baby for cord-blood withdrawal.;Patients: HIV-1-infected pregnant women and their newborn baby for cord-blood withdrawal.

Exclusion criteria

Healthy subjects:
1. infected with a (chronic) infection
2. immune system altering disease
3. immune system altering medication;Healthy and HIV-1-infected mothers:
4. preterm delivery at less than 33 weeks

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:	Pending
Start date (anticipated):	01-12-2006
Enrollment:	20

Type:	Anticipated

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	NL14795.018.06