Immunity of the placenta and newborns

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1. To investigate the influence of different immunosuppressive drugs on the immune response of placental derived mononuclear cells, peripheral blood derived mononuclear cells, and cord blood derived mononuclear cells.2. To investigate the neonatal...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON44239

Source
ToetsingOnline

Brief title
APeN

Condition

- Other condition
- Pregnancy, labour, delivery and postpartum conditions

Synonym
immunsuppressive therapy during pregnancy

Health condition

neonatale immuunontwikkeling

Research involving
Human

Sponsors and support

Primary sponsor: Kindergeneeskunde, Radboudumc
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cord blood, Immunity, Placenta, Pregnancy

Outcome measures

Primary outcome

1. To investigate the influence of different immunosuppressive drugs on the

immune response of placental derived mononuclear cells, peripheral blood

derived mononuclear cells, and cord blood derived mononuclear cells.

2. To investigate the neonatal immune response against a variety of pathogens

and compare this with the adult immune response

Secondary outcome

na

Study description

Background summary

This protocol will entail two different projects. The first project (1) investigates the effects of immunosuppressive drugs on immune cells of the placenta, cord blood, and peripheral maternal blood during pregnancy and postnatally. The second project (2) investigates the innate immune response of newborns.

1. Investigation of the effect of immunosuppressive drugs on placental derived mononuclear cells, peripheral blood derived mononuclear cells during pregnancy and postnatally, and cord blood derived mononuclear cells

It is now well accepted that the immune system plays an important role in the implantation of the developing semi-allogeneic embryo into the wall of the maternal uterus. The immune system has to balance the opposing needs of maintaining robust immune reactivity to protect both mother and fetus from invading pathogens, while at the same time tolerating highly immunogenic paternal alloantigens in order to sustain fetal integrity. In fertile women the

endometrium prepares every month for potential pregnancy. In the final part of the menstrual cycle there is a huge influx of maternal leucocytes, including a high percentage of NK cells. These uterine NK cells (uNK) direct placentation by controlling trophoblast invasion and regulatory T cells are responsible for the establishment of tolerance by modulating the immune response. A variety of other cell types, including decidual stromal cells, dendritic cells, and immunomodulatory multipotent mesenchymal stromal cells, are found at the fetal* maternal interface. These cells conspire to establish a suitable environment for fetal development without compromising systemic immunity. Defects in any of these components can lead to gestational failure despite successful fertilization. Since immunosuppressive drugs can affect immune cells, they are likely to affect immune cells at the fetal-maternal interface with subsequent complications for pregnancy such as preeclampsia, preterm delivery and fetal growth restriction.
These complications are commonly observed in renal transplant patients. Here we will investigate the in vitro effect of different immunosuppressive drugs on placental derived mononuclear cells from healthy pregnant women. The in vivo effects of immunosuppressive medication will be studied by obtaining the placenta of pregnant kidney transplant patients. Also, the effects of the use of immunosuppressive drugs, such as calcineurin inhibitors and azathioprine, in these pregnant patients may be visible in the peripheral blood compartment and neonatal blood compartment. Therefore, we will also study the in vivo effect of these drugs on maternal peripheral blood derived mononuclear cells taken at each trimester during pregnancy (*8-13 weeks, *25 weeks of pregnancy, around labor (*36-40 weeks), and 8-10 weeks postnatally) and on cord blood derived mononuclear cells. The results will improve our insights on the risks of immunosuppressive drugs on pregnancy in renal transplant patients and on their offspring.

2. Investigation of the innate immune response of newborns:

The development of the immune system takes place in the first months of life during which infants are particularly vulnerable to viral and bacterial infectious diseases. The introduction of the national vaccination program significantly reduced the burden of infectious diseases in the pediatric population. However, young infants are still susceptible to infectious due to the fact that most vaccines are administered after 2 months. Secondly, for many pathogens there is currently a lack of (optimal) vaccines. A small percentage of all infants develop a severe infection and require hospitalization and/or mechanical ventilation. The exact mechanisms of the susceptibility to develop a severe infection are yet to be elucidated. In this context, collection of cord blood will allow investigation of the neonatal immune response. Better understanding of the neonatal immune response will proof useful in elucidating the pathogenesis of infectious diseases.

Study objective

1. To investigate the influence of different immunosuppressive drugs on the immune response of placental derived mononuclear cells, peripheral blood derived mononuclear cells, and cord blood derived mononuclear cells.

2. To investigate the neonatal immune response against a variety of pathogens and compare this with the adult immune response

Study design

This is an in vitro study to investigate (1) the effects of immunosuppressive drugs on immune cells of the placenta, maternal peripheral blood, and cord blood, and (2) the neonatal immune response against a variety of pathogens. This study will be coordinated by the Laboratory of Pediatric Infectious Diseases at the Department of Pediatrics of the Radboud University Medical Center and the Laboratory of Medical Immunology at the Radboud University Medical Center.

Pregnant women who attend the Department of Gynaecology and Obstetrics of the Radboud University Medical Center will be included in the study. The physician determines whether the pregnant women are eligible to be included in the study and will inform the subjects about the study.
After informed consent, the placenta will be taken immediately after the caesarean section. The amount of cord blood taken will usually vary between 10 en 200 ml of blood depending on the size of the placenta. The placenta will be placed in a tray and 500 ml of cold PBS will be added for preservation.
For the renal transplant patients and some healthy controls, collection of maternal blood in EDTA tubes (at gestational week 8-13, week 24, at term pregnancy (*36-40 weeks), and 8-10 weeks postnatally) will be planned during regular visits to the hospital and at delivery, and if possible with regular patient care collection. A case record form is used to gather information about medical history, gestational age and use of immunosuppressive medication.

Study burden and risks

In this study, peripheral blood, placenta tissue and blood from the placenta will be used. There are no direct benefits of this study for the participating subjects. The benefits may be related to the future understanding of effects of immunosuppressive drugs on the maternal immune system and placenta and future understanding neonatal immune responses. Because peripheral blood will be collected during a regular visit to the clinic and only the placenta is used in this process, there is no direct risk to the subject.

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 pregnant women aged 18-40 years.;Kidney transplant >1 year before pregnancy
Stable kidney function glomerular filtration rate of >30ml/min/1.73m2

Exclusion criteria

Healthy:
Use of immunosuppressive drugs, biological or antidepressants
HIV positivity
Active infection during caesarean section
o Signs of infection (maternal fever or signs of intrauterine infection)
o Use of antibiotics prior to caesarean section;Patients
Use of other medication (biologicals or antidepressants) besides immunosuppressive medication
HIV positivity

Active infection during delivery
o Signs of infection (maternal fever or signs of intrauterine infection)
o Use of antibiotics prior to caesarean section

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:	Recruiting
Start date (anticipated):	02-01-2018
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	07-11-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-04-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-05-2021
Application type:	Amendment

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL62556.091.17