BMI dependent regulation of macrophages and monocytes in pregnancy

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Primary Objective: analyse the effect of maternal BMI on levels of macrophage cell and monocyte subsets in decidual tissue and maternal blood. Secondary Objective: analyse differences in the effect of maternal blood stimulation with conditioned…

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

Summary

ID

NL-OMON48238

Source
ToetsingOnline

Brief title
BMI, macrophages and pregnancy

Condition

- Immune disorders NEC
- Pregnancy, labour, delivery and postpartum conditions

Synonym
being fat, Obesity

Research involving
Human

Sponsors and support

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

Intervention

Keyword: BMI, Macrophages, Obese, Pregnancy

Outcome measures

Primary outcome

Primary parameters will be the effects of maternal BMI on levels of macrophage cell and monocyte subsets in decidual tissue and maternal blood.

Secondary outcome

Secondary parameters will be the differences in the effect of maternal blood stimulation with conditioned medium of adipose tissue and LPS and differences in monocyte subsets in umbilical cord blood.

Study description

Background summary

Adaptation of the maternal immune system to accommodate the semi-allogeneic fetus is necessary for pregnancy success. Dysregulation of the maternal immune adaptation is implicated in reproductive disorders such as infertility, recurrent miscarriage, fetal growth restriction, and preeclampsia, which together affect at least 25% of women in the reproductive age. The exact mechanisms being responsible for fetal tolerance are not known, however T cells, natural killer (NK) cells, monocytes, and macrophages are all regarded as important players in the adaptation of the maternal immune response.

Several factors are known to influence pregnancy outcome, including obesity. During pregnancy, obesity is associated with various unfavorable pregnancy outcomes, such as: spontaneous miscarriage, congenital anomalies, preeclampsia, and fetal macrosomia. Thus far, the biological mechanisms behind the association between obesity and unfavorable pregnancy outcomes are only partly understood. Possibly, a disturbed maternal immune balance, such as altered macrophage characteristics are involved in the complicated pregnancy outcomes. Our previous study indicated altered macrophages subsets in the decidua in women with a BMI >30.

Whether these cells are functionally altered, or whether macrophage precursor

cells within blood (monocytes) are altered in women with a BMI >30 is not known. Evidence indicates that the polarization in monocyte subsets is also dependent on the local tissue environment in which they differentiate. Adipose tissue produces immune active substances as cytokines and complement factors which might influence the polarization of monocytes and macrophages. Monocytes and adipose tissue come in close contact with each other and therefore might local adipose tissue environments influence systemic monocyte differentiation. We will analyse this by using flowcytometry, functionality tests and rtPCR on postpartum placental tissues, maternal peripheral blood and umbilical cord blood.

We hypothesize that in pregnancies with women with a BMI >30, the maternal immune system is differently activated (less tolerant) compared to women with a BMI <25.

Study objective

Primary Objective: analyse the effect of maternal BMI on levels of macrophage cell and monocyte subsets in decidual tissue and maternal blood. Secondary Objective: analyse differences in the effect of maternal blood stimulation with conditioned medium of adipose tissue and LPS and differences in monocyte subsets in umbilical cord blood.

Study design

This study is an observational study in which levels of monocytes and macrophages will be analysed. Both pregnant women with a BMI>30 and with a BMI between 19-25 will be included. Levels of monocyte subsets will be analysed in maternal blood (obtained around 12 and 30 weeks pregnancy and around delivery, and umbilical cord blood).

Furthermore, maternal peripheral blood will be stimulated. Adipose tissue for the stimulation of monocytes will be derived from visceral and subcutaneous biopsies, taken during caesarean section. Adipose tissue will be cultured for one day and analysed and supernatant of the conditioned medium will be added to the monocytes. Monocytes will be cultured consequently for 6 days in the presence of growth factors which turn the monocytes into macrophages.

Macrophages will be derived from decidual biopts, taken from the placenta after delivery and from the stimulation of monocytes with adipose tissue. They will be analysed using multicolour flowcytometry and RT-PCR. Levels and subsets of macrophages and its deriving cytokines will be analysed.

If possible maternal blood will be taken during routine blood sampling around 12 and 30 weeks of pregnancy and around delivery, and cord blood will be taken after fetal cord clamping.

Study burden and risks

Placental sampling does not carry any risk for the women. If possible, maternal blood will be taken during routine blood sampling and cord blood will be taken after fetal cord clamping this will not pose any risk on the individuals. The adipose tissue biopsies will be collected during caesarean sections on tissue which is already visible during the operation. The adipose tissue retrieval can cause bleeding of the tissue but this risk is very small and the surgeon monitors the sampling size while performing the operation. In comparison with the caesarean section the risk of taken biopsies is negligible. Participation in this study will not benefit the women personally. However, the present study investigates the maternal immune system during pregnancy. Knowledge about the pathogenesis of immune related complications of pregnancy may in the long term benefit any pregnant woman.

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

- written informed consent
- 18-40 years
- BMI >30 or BMI >19 - <25
- Pregnant

Exclusion criteria

smoking
- immune related disorders
- fever / illness within the last month
- fertility treatment (ovulation induction, intra-uterine insemination, IVF-ICSI)
- BMI <19

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-09-2019
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	03-06-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-09-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL69475.042.19