Maternal and fetal/neonatal pharmacokinetics and - dynamics of corticosteroids during pregnancy as treatment for fetal lung maturation

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To examine the pharmacokinetics in maternal blood of standard regimen at the Erasmus MC of two doses of 12 mg betamethasone intramuscular with a 24 hours interval for pregnant women suspected of preterm birth with a gestational age between 23+5...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Pregnancy, labour, delivery and postpartum conditions
Study type	Observational invasive

Summary

ID

NL-OMON56400

Source
ToetsingOnline

Brief title
MaDyCo-study

Condition

- Pregnancy, labour, delivery and postpartum conditions

Synonym
premature contractions, Preterm birth

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Betamethasone, Dexamethasone, Pharmacokinetics, Suspicion of preterm birth

Outcome measures

Primary outcome

To examine the maternal and fetal (as measured in umbilical cord blood sampling directly after birth) pharmacokinetics of standard regimen at the Erasmus MC of two doses of 12 mg betamethasone intramuscular with a 24 hours interval for pregnant women suspected of preterm birth with a gestational age between 23+5 until 33+6 weeks. Farmacokinetic parameters, which will be determined are: distribution (VD), clearance (Cl), elimination-rate constant (kel), steady-state concentration (Css), half-life (t1/2), bioavailability (F).

Secondary outcome

- To examine the relation between CUYP3A4 genotype and the pharmacokinetics of the primary objective.

- To examine the relation between maternal age and the pharmacokinetics of the primary objective.

- To examine the relation between fetal sex and the pharmacokinetics of the primary objective.

- To examine the relation between maternal weight/BMI and the pharmacokinetics of the primary objective.

- To examine the relation between the number of fetus and the pharmacokinetics of the primary objective

- To examine the relation between parity the pharmacokinetics of the primary

objective.

- To examine the relation between pre-eclampsia and the pharmacokinetics of the primary objective

- To examine the relation between oestradiol on pharmacokinetics of the primary objective

- To examine the relation between pharmacokinetics in cord blood and neonatal blood

Study description

Background summary

Improving pregnancy outcome is essential in improving health of both parents and their offspring during the life course. Preterm birth (PTB) occurs in 10-15% of all pregnancies, is the leading cause of perinatal mortality and morbidity {Goldenberg, 2008 #6}, has long-term adverse consequences for postnatal health {Huddy, 2001 #8} and is a burden for health care expenditure. In order to improve neonatal outcome, antenatal corticosteroids (ACS) are routinely administered to women at risk for preterm delivery before 34 weeks of pregnancy. {Jobe, 2018 #2;Roberts, 2017 #3;Travers, 2018 #1} However, the current, worldwide standard of care, for the use of ACS is still based on animal experiments performed in the 1970*s. {Liggins, 1969 #4} Although ACS treatment to improve neonatal outcome was clinically introduced in the 70*s, still only two dosing regimens are used, neither of which have been investigated, re-evaluated or refined to determine the optimal doses or treatment interval. With the current health care approach of personalized medicine in mind, the same universal approach for everybody, independent of gestational age, number of fetus, maternal weight or comorbidity one dose does not fit all since it often has not the desired effect. Due to the lack of optimization of the above mentioned synthetic corticosteroid drug regimens {Kemp, 2019 #5}, significant gaps in knowledge exist. An important aspect to set up, investigate and understand dosing and also dosing interval experiments, is knowledge of the maternal individual pharmacokinetics and pharmacogenetics of the drug of interest during pregnancy. As an example, synthetic corticosteroids are eliminated by the liver by action of the enzyme cytochrome P450 (CYP) 3A4 and variations of Single Nucleotide Polymorphisms (SNPs) in the CYP3A4 gene will result in different drug effects and even adverse effects.

Study objective

To examine the pharmacokinetics in maternal blood of standard regimen at the Erasmus MC of two doses of 12 mg betamethasone intramuscular with a 24 hours interval for pregnant women suspected of preterm birth with a gestational age between 23+5 until 33+6 weeks.

Study design

A clinical observational pilot study.

Study burden and risks

For all participants the extra burden will be the insertion of an intravenous canule that will solely be used for blood sample collection. After each administration of antenatal steroids, blood samples (1 ml, 1 EDTA tube) will be collected in sampling time windows according to a schedule.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Newborns

Inclusion criteria

1) Older than 18 years of age.
2) Admitted at the Department of Obstetrics at Erasmus MC - Sophia for suspicion of preterm birth with a gestational age of 23+5 weeks until 33+6 weeks.
3) Understanding of Dutch in speaking and reading.
4) Written informed consent.

In order for the neonate to be able to participate in this study, the parent must meet the following criteria:
5) Older than 18 years of age.
6) Admitted at the Department of Obstetrics at Erasmus MC - Sophia for suspicion of preterm birth with a gestational age of 23+5 weeks until 33+6 weeks.
7) Understanding of Dutch in speaking and reading.
8) Written informed consent for the neonate.

Exclusion criteria

1) Women unable or unwilling to agree with the procedures.
2) Women unable or unwilling to give written informed consent.
3) Women with acute obstetric complications requiring immediate delivery at time of admission.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2021
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO Date:	19-12-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-04-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-08-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL71592.078.19
Other	NL9318