Pilot study: The influence of commonly used medicines in obstetric care on the fetal ECG
Short title: FEMME (Fetal Ecg and Maternal MEdication)

Published: 27-02-2013
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To validate spectral analysis of the fHRV as a new method for fetal monitoring. To determine the exact influence on fHRV of several commonly used medicines in obstetric care; namely tocolytic drugs, corticosteroids, antihypertensive agents,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Maternal complications of pregnancy
Study type	Observational non invasive

Summary

ID

NL-OMON43800

Source
ToetsingOnline

Brief title
FEMME (Fetal Ecg and Maternal MEdication)

Condition

- Maternal complications of pregnancy

Synonym
Complications during pregnancy

Research involving
Human

Sponsors and support

Primary sponsor: Maxima Medisch Centrum
Source(s) of monetary or material Support: Er is geen financiering voor dit ondrzoek.

Intervention

Keyword: Electrofetal monitoring, Fetal ECG, fHRV, Medication

Outcome measures

Primary outcome

Measurements are performed using ten self-adhesive electrodes, placed in a fixed configuration on the maternal abdomen. A non-invasive electrophysiologic monitor for obstetrics (NEMO), is used to record and store the electrical activity on the maternal abdomen. The collected data will be analysed off-line. The maternal electrocardiogram (ECG) is removed, without affecting the present fECG-complexes. Sympathetic and parasympathetic activity are determined by calculating the power in the low frequency (LF; 0.04-0.15 Hz) and high frequency (HF; 0.4-1.5 Hz) spectral band, respectively. This energy can be expressed in absolute units (LF and HF) or normalised units (LFn and HFn); for more information; see protocol page 9.

We will conduct a baseline measurement (*0-measurement*), before administration of the medicine or, when this is not feasible, after the effects of the medicine is vanished. This will be determined by the half-life of the specific medicine (for more information, see protocol chapter 3, page 11). Measurements will be repeated at established time intervals, depending on the pharmacokinetics of the specific medicine.

The primary study parameters are the differences in LF, LFn, HF, HFn and LF/HF-ratio, that manifest in the measurements before and after administration of the medicine. The expected changes are different for every used medicine, and because of the lack of prior studies it is hard to predict these changes. Because the measurements take 30-45 minutes, it is unlikely that these differences are solely caused by fetal behavioural stages, fetal body movements or compression of the umbilical cord.

Secondary outcome

As secondary analysis, we will conduct measurements of the maternal electrohysterogram. This will be extracted from a electrode patch, placed on the maternal abdomen. We will analyse the effect of the medication on the uterine activity.

Postpartum, general information regarding the delivery will be obtained from the obstetric caregiver at the time of delivery. This will be noted on a separate *follow-up postpartum* file and constitutes the inclusion number of the patient, date of birth of the child, gestational age at birth, birth weight, sex, Apgar score (1, 5 and 10 minute score), postpartum events and cardiac problems postpartum.

Study description

Background summary

Cardiotocography (CTG), the current method for fetal monitoring worldwide, has a poor predictive value with regard to the detection of neonatal asphyxia.

There is an urgent need for a fetal surveillance method that provides reliable information on fetal wellbeing, to prevent perinatal morbidity and mortality. This method should obtain data non-invasively, so it can be applied antepartum as well as durante partu and in fetuses in breech presentation. Especially in (high risk) fetuses at risk for premature birth, the CTG is often indecisive and reliable information on fetal wellbeing is important.

Recent research showed that additional information on fetal wellbeing can be obtained by using spectral analysis of fetal beat-to-beat heart rate variability (fHRV), calculated from non-invasive fetal electrocardiogram (fECG) recordings. Hypoxia activates the autonomic nervous system, which modulates the fetal heart rate (FHR). The low-frequency (LF)-component is both sympathetically and parasympathetically mediated. The high-frequency (HF)-component is solely parasympathetically mediated. The ratio LF/HF-power provides a marker of the sympatho-vagal balance in the control of heart rate, and can be used to monitor autonomic nervous system activity.

Spectral analysis of the fHRV seems to be a promising new field in antenatal monitoring, but needs to be validated properly before its introduction in clinical practice. An important aspect is the influence on fHRV of commonly used medicines in obstetric care; amongst others tocolytic drugs, corticosteroids, antihypertensive agents, medication used for sedation and pain relief during labour.

Study objective

To validate spectral analysis of the fHRV as a new method for fetal monitoring. To determine the exact influence on fHRV of several commonly used medicines in obstetric care; namely tocolytic drugs, corticosteroids, antihypertensive agents, medication used for sedation and pain relief during labour.

Study design

At first, this study will be performed as an observational pilot study, because there is very little former research regarding the influence of tocolytic drugs, corticosteroids, antihypertensive agents, medication used for sedation or pain relief during labour on the spectral analysis of the fHRV. Later on, a prospective longitudinal study will be designed.

Study burden and risks

There are no physical risks or side effects to the mother, fetus or third parties. Allergy or irritation from the used electrodes is the only conceivable problem as this is the only contact of the subject with the equipment. All of the used equipment is approved by the Medical Technical Service Department of the MMC in safety tests. In pregnant women, one must always bear in mind the

risk of aortocaval compression. From midpregnancy onwards, the enlarged uterus compresses both the inferior vena cava ant the lower aorta when the patient is lying in supine position(34). To prevent this from happening, the patient will be placed in a semi-recumbent position or left lateral tilt position during the measurements.

Sometimes patients are discharged from the Máxima Medical Center before completion of the total study period (5 days in case of corticosteroid administration). We will ask these patients if they want to participate in performing the remainder of the measurements at their home or the hospital they are referred to, in order to complete the study period.

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

Pregnant women, carrying a healthy, singleton fetus with a gestational age between 20 and 42 weeks, receiving one or more of the following medicines; tocolytic drugs, corticosteroids, antihypertensive agents or medication for sedation or pain relief during labour. Patients receiving both tocolytic drugs and corticosteroids at the same time can participate in this study, since this is standard care nowadays. Also patients receiving antihypertensive agents and corticosteroids simultaneously can be included in this study. In this way, we will get information that is applicable in daily clinical practice.

Exclusion criteria

Women under the age of 18 years old, using other medicines than examined in this study, multiple pregnancies, women carrying a fetus with a known congenital malformation and fetuses with an intra-uterine growth restriction are excluded (defined as a fetal growth lower than p5 as estimated by echography). Fetal congenital malformations discovered after inclusion will be analysed separately.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-03-2013
Enrollment:	750
Type:	Actual

Ethics review

Approved WMO

Date:	27-02-2013
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	08-05-2013
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	07-11-2013
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	15-06-2015
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	30-05-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	NL43294.015.13