To study the cardiovasculair effects of vasodilatation by nifedipine (Adalat gastrointestinal therapeutic system) with or without plasma volume expansion with Voluven (colloid) in women with preeclampsia

Published: 31-07-2006
Last updated: 14-05-2024

The first aim is to study the cardiovascular effects of nifedipine in pregnancy in patients with preeclampsia. Our second aim is to answer the following questions:Does Adalat GITS with plasmavolume expansion in patients with preeclampsia, lead...

Ethical review	Approved WMO
Status	Pending
Health condition type	Maternal complications of pregnancy
Study type	Observational invasive

Summary

ID

NL-OMON29982

Source
ToetsingOnline

Brief title
plasmavolumeexpansion, nifedipine and preeclampsia

Condition

- Maternal complications of pregnancy

Synonym
preeclampsia, toxicosis

Research involving

Human

Sponsors and support

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

Intervention

Keyword: cardiac output, nifedipine, plasma volume expansion, preeclampsia

Outcome measures

Primary outcome

Cardiovascular variabels: systolic, diastolic and mean bloodpressure, oxygen saturation, pulse and cardiac output (and the systemic vascular resistance).

Plasmavolume-measurement.

Secondary outcome

Hemoglobin, Thrombocytes, MCV, Na, K, Urate, Urea, Kreatinine, Glucose, ALAT, ASAT, LDH, Calcium, albumin, Mg, haptoglobine, lactate, total proteine,

arterial bloodgas

Cardiotocography: baseline and variability of the fetal hart as a way of assessing the fetal condition.

Echoscopic measurements: doppler pulsatility index of the uterina arteries, umbilical and middle cerebral arteries

Nifedipine-serum concentrations at different times, to calculate an area under the curve (AUC).

Protein-kreatinine ratio in the urine to assess proteinuria.

Study description

Background summary

Nifedipine is a calciumantagonist used in obstetrics off-label as an anti-hypertensive drug as well as for premature labour.
Despite its frequent use the hemodynamic effects in pregnancy are only partially known.
In preeclampsia the maternal circulation is characterized by an increased bloodpressure and an increased systemic vascular resistance, a decreased cardiac output and a decreased circulating plasma volume. Correction of the circulating volume by plasma volume expansion only, does not result in a significant bloodpressure drop or other improvement of the maternal or foetal condition.
Reduction of the arterial systemic resistance by nifedipine leads to a substantial reduction of the bloodpressure en increase of the cardiac output. An uncontrolled reduction of the bloodpressure can lead to uterine hypoperfusion and foetal distress. The combination of both strategies, plasma volume expansion together with vasodilatation by dihydralazine, has been used succesfully for years. In the UMCN and other hospitals, nifedipine has been used extensively as capsules as well as in the longacting GITS formulation. However the pharmacodynamics of Adalat GITS have not been extensively studied during pregnancy with or without plasma volume expansion. In view of the daily use of Adalat GITS in pregnancy we think it is necessary to do so. Also there is a lack of pharmacokinetic data on Adalat GITS think in pregnancy .

Study objective

The first aim is to study the cardiovascular effects of nifedipine in pregnancy in patients with preeclampsia.

Our second aim is to answer the following questions:
Does Adalat GITS with plasmavolume expansion in patients with preeclampsia, lead significantly more often to a desired (ca 20%), controlled, reduction of the peripheral vascular resistance (calculated from the mean arterial pressure and the cardiac output) than without plasmavolume expansion?

Secundairy aims:
1. Does Adalat GITS with plasmavolume expansion in patients with preeclampsia lead less often to a change in the doppler flow profiles of the uterina artery, the variability of the foetal hartrhythm, as a sign of changed uterine perfusion?
2. Characterization of the pharmocokinetics in patients with preeclampsia of Adalat GITS with or without plasmavolume expansion?

Study design

Prospective randomised, unblinded study in pregnant women with preeclampsia in whom vasodilatation is established by Adalat GITS with or without plasmavolume expansion by 500 ml Voluven.

Study burden and risks

It is comparable with a routine hospital admission.
the extra burden consists mainly of the more frequent registration of the bloodpressure, saturation and pulse. The bloodpressure will be measured invasively via an intraarterial catheter. The cardiac output will be measured with Innocor, an apparatus that uses the measurement of sulfahexafluoride, an insoluble gas that is harmless, during inspiration and expiration, using the Fick principle. The cardiovascular measurements will be performed 10 times at 2, 4, 6, 8, 12, 16, 24, 36, 48 hours.
There will be two additional ultrasound examinations apart from the routine ultrasound examination.
Regarding the plasma volume measurement: routine intravenous excess; 20 cc of dextraan 70 will be administered and at different times a serumsample will be drawn from the arterial line at 10, 20 and 30 minutes. This test will be repeated at 24 hours. At the protocol-times of (0), 2, 4, 8, 16, 24, 48 hours a bloodsample will be taken for determination the nifedipine serumconcentration.
Instead of a cardiotocogram twice in 48 hours, an additional 8 ctg's will be performed for 30 minutes each

Contacts

Public
Academisch Medisch Centrum

Kastanjelaan 44
6533 BD Nijmegen
Nederland
Scientific
Academisch Medisch Centrum

Kastanjelaan 44
6533 BD Nijmegen
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

preeclampsia, gestational age 24- 34 weeks, singleton pregnancy

Exclusion criteria

known allergy to nifedipine, known cardiovasculair or renal- or liverpathology, previous treatment with antihypertensives or tocolytics, foetal distress necessitating delivery in less than 48 uur, imminent eclampsia, no informed consent from the patient or the doctor treating the patient, multiple pregnancy, unable to take tablets

Study design

Design

Study phase:	3
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2006
Enrollment:	22
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Adalat GITS
Generic name:	nifedipine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	31-07-2006
Application type:	First submission
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
EudraCT	EUCTR2006-003143-23-NL

Register	ID
CCMO	NL11764.091.06