# Maternal pharmacokinetics and pharmacodynamics of nicardipine (iv) during treatment of severe hypertension in pregnancy.

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Our aim is to determine a Pharmacokinetic/Pharmacodynamic (PkPd) based dosing model for nicardipine used for treatment of severe hypertension in preeclamptic patients. The model is based upon determination of maternal, fetal and neonatal plasma...

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

## Summary

### ID

NL-OMON36863

**Source**
ToetsingOnline

**Brief title**
Nicardipine PkPd study

### Condition

- Maternal complications of pregnancy
- Vascular hypertensive disorders

**Synonym**
preeclampsia

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam
**Source(s) of monetary or material Support:** geen geldstroom;geen financiering

## Intervention

**Keyword:** nicardipine, pregnancy, severe hypertension, treatment

## Outcome measures

### Primary outcome

Maternal first half life (1st 24 hours after initiation), second half life (24hours after administration), distribution half time, elimination half time, assessing risk of accumulation. Changes in blood pressure, heart rate, cardiac output, cardiac index, stroke volume, peripheral resistance, and NT-proBNP values after administration of nicardipine.

### Secondary outcome

Determine concentration gradient to breastmilk. Determine pharmacokinetic parameters in the neonate and if appropriate correlate neonatal pharmacokinetic parameters to neonatal pharmacodynamic changes. Exploring haemodynamic changes in preeclamptic patients with severe hypertension and exploring the haemodynamic transfer to normal in the puerperium.

# Study description

### Background summary

Nicardipine is a very effective treatment for severe hypertension in pregnancy and is increasingly considered as first line treatment option in many obstetric wards in the Netherlands. No maternal pharmacokinetic and pharmacodynamic data are available, which are necessary for the development of an optimal dosage schedule and for safety aspects of the mother, the fetus and neonate. This is a

field that needs to be explored.

### Study objective

Our aim is to determine a Pharmacokinetic/Pharmacodynamic (PkPd) based dosing model for nicardipine used for treatment of severe hypertension in preeclamptic patients. The model is based upon determination of maternal, fetal and neonatal plasma levels of nicardipine, and the corresponding changes in maternal haemodynamic parameters after administration of nicardipine.

### Study design

prospective observational study.

### Study burden and risks

Since many years nicardipine is the option of 1st choice (in the Isala Clinics and Erasmus University Hospital Rotterdam) for treatment of severe hypertension in pregnancy. Nicardipine showed to be very effective and no severe maternal or fetal complications due to continuous treatment with nicardipine occurred (data being analysed). Review of the literature on this subject shows significant decrease in systolic and diastolic blood pressure in all patients with no severe maternal or fetal complications. Still only limited data are available of intravenous use of nicardipine for treatment of severe hypertension in pregnancy, and further research is needed to provide the best dose response ratio for nicardipine used for treatment of severe hypertension in pregnancy. Risk of study participation is negligible. All patients receive nicardipine treatment as part of standard clinical care. Blood samples (1mL) will be taken from an intra-arterial catheter. Blood pressure in the patients is and will be monitored via an intra-arterial catheter, which avoids repetitive venous bloodsampling. Other haemodynamic parameters will be determined using non-invasive arterial pressure waveform analysis (Finapres®).

## 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 patients with preeclampsia (hypertension and protein/creatinine ratio >= 30mg/mmol or >= 300mg protein/24hours) complicated with severe hypertension (systolic bloodpressure >= 160mmHg and/or diastolic blood pressure >= 110mmHg);gestational age >= 20 weeks;working knowledge of Dutch language

## Exclusion criteria

Fetal indication for immediate delivery, ie. signs of fetal distress: spontaneous repeated persistent unprovoked decelerations on CTG;Fetal death or major fetal congenital anomalies or estimated fetal weight below 500 grams;Placental abruption;Concomitant medication: nifedipine, cimetidine, labetalol;Clinically relevant pulmonary edema, defined as clinically relevant respiratory failure or severe respiratory distress requiring oxygen supplementation (more than 10 litres), with rales and/or pulse oximetry of <94% on room air;Eclampsia;Suspicion of (sub)capsular liverhematoma on physical examination;Renal failure (creatinine clearance < 40 mL/min)
• Suspicion of cerebro-vascular incident on physical examination
• Suspicion of trombo-embolism on physical examination
• Other severe maternal complications
• Maternal age <16 years
• Mentally incapacitated patient
• Impossible to place an intra-arterial catheter.

# Study design

## Design

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| Study phase: | 2 |
| Study type: | Observational non invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-07-2014 |
| Enrollment: | 40 |
| Type: | Anticipated |

## Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Cardene |
| Generic name: | nicardipine |
| Registration: | Yes - NL outside intended use |

# Ethics review

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| Approved WMO Date: | 13-03-2013 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 14-03-2013 |
| Application type: | First submission |

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 |
|---|---|
| EudraCT | EUCTR2012-005330-10-NL |
| CCMO | NL42054.075.12 |