# Perinatal allopurinol trial for reduction of birth asphyxia induced brain damage.

No registrations found.

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|---|---|
| **Ethical review** | Positive opinion |
| **Status** | Recruitment stopped |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON28692

**Source**
Nationaal Trial Register

**Brief title**
ALLO-trial

**Health condition**

perinatal asphyxia, neuroprotection, allopurinol, newborn, oxidative stress

### Sponsors and support

**Primary sponsor:** Prof dr. F. van Bel
**Source(s) of monetary or material Support:** ZonMW

### Intervention

### Outcome measures

**Primary outcome**

The brain damage marker S100B and the severity of oxidative stress measured in umbilical cord blood and neonatal blood (isoprostane, neuroprostane, non protein bound iron).

**Secondary outcome**

Neonatal mortality and serious composite morbidity.

# Study description

**Background summary**

OBJECTIVE:

Hypoxic-ischaemic encephalopathy is associated with development of cerebral palsy and cognitive disability later in life, and is therefore one of the fundamental problems in perinatal medicine.
The xanthine-oxidase inhibitor Allopurinol (ALLO) reduces the production of free radical formation, thereby limiting the amount of hypoxia-reperfusion damage. Animal and human studies suggest that administration of ALLO immediately prior to delivery in the case of suspected intra-uterine asphyxia might reduce hypoxic-ischaemic encephalopathy. In the present proposal, we aim to answer whether perinatal llopurinol administration does reduce hypoxic-ischaemic encephalopathy in neonates exposed to intra-uterine asphyxia

STUDY DESIGN:
Randomized double blind placebo controlled multicenter study

STUDY POPULATION:
Labouring women at term in whom the fetus is suspected of intra-uterine asphyxia

INTERVENTION:
Allopurinol or placebo administration antenatally to the mother.

OUTCOME MEASURES:
Primary outcome measure is severity of oxidative stress as measured in umbilical cord blood and neonatal blood (isoprostane, neuroprostane, non protein bound iron and S100B).
Secondary outcomes are neonatal mortality and serious composite morbidity.

SAMPLE SIZE CALCULATION AND DATA-ANALYSIS:
110 patients per group are needed (a total of 220 patients) if based on a reduction in clinical levels of oxidative stress (isoprostane/ neuroprostane) of 10%, using a two sided test (alpha 0,05, power of 0.80).

ECONOMIC EVALUATION:
As the costs of ALLO and its administration are relatively low, a small treatment effect will already make the intervention cost-effective. We will perform economic modelling, in which we assess at what prevalence of encephalopathy administration of ALLO is cost-effective.

### Study objective

Fetuses with hypoxia-ischemia, as indicated by the STAN S21 monitor ST elevations or abnormalities on cardiotocography (CTG), whose mothers are subsequently prenatally treated with 500 mg (iv) allopurinol will have a reduction in free radical-induced post-asphyxial reperfusion damage of brain and heart. Furthermore, they will have a better neurological outcome as compared to placebo-treated neonates.

### Study design

- Prim: immediately at birth

- Sec: 2 years of age

### Intervention

Randomized, double blind controlled allopuirnol (500mg iv) or placebo as soon as fetal hypoxia is imminent

## Contacts

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# Eligibility criteria

## Inclusion criteria

1. Gestational age of 36 weeks or more, determined by maternal dates and/or Ballard score.

2. Objective fetal hypoxia registered by:

- Abnormalities on STAN S21 fetal electrocardiography monitor (Neoventa Medical, Gothenborg, Sweden). A fetal scalp electrode is allocated to the parturient for continuous internal cardiotocographic recordings combined with the computer for fetal heart monitor for ST analysis of the fetal electrocardiogram signals, which are stored automatically in digital form OR

- non-reassuring CTG

- Fetal blood sampling: pH<7.20

3. Informed consent given by patient.

## Exclusion criteria

1. Congenital, chromosomal or syndromal malformations.

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |

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| Masking: | Double blinded (masking used) |
| Control: | Placebo |

### Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-01-2009 |
| Enrollment: | 220 |
| Type: | Actual |

## Ethics review

Positive opinion

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| Date: | 16-07-2008 |
| Application type: | First submission |

## Study registrations

### Followed up by the following (possibly more current) registration

ID: 36929
Bron: ToetsingOnline
Titel:

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

| Register | ID |
|---|---|
| NTR-new | NL1328 |
| NTR-old | NTR1383 |
| CCMO | NL26516.000.09 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd |
| OMON | NL-OMON36929 |

# Study results

**Summary results**

Van Bel F, Shadid M, Moison RM, Dorrepaal CA, Fontijn J, Monteiro L, Van De Bor M, Berger HM. Effect of allopurinol on postasphyxial free radical formation, cerebral hemodynamics, and electrical brain activity. Pediatrics. 1998 Feb;101(2):185-93.
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Shadid M, Moison R, Steendijk P, Hiltermann L, Berger HM, van Bel F. The effect of antioxidative combination therapy on post hypoxic-ischemic perfusion, metabolism, and electrical activity of the newborn brain. Pediatr Res. 1998 Jul;44(1):119-24.<br><br>
Benders MJ, Bos AF, RademakerCM etal. Early postnatal allurinol does not improve short term outcome after severe birth asphyxia. Arch Dis Child Fetal neonatal Ed 2006:91:163-165
<br><br>
Kaandorp JJ, Benders MJ, Rademaker CM, Torrance HL, Oudijk MA, de Haan TR, Bloemenkamp KW, Rijken M, van Pampus MG, Bos AF, Porath MM, Oetomo SB, Willekes C, Gavilanes AW, Wouters MG, van Elburg RM, Huisjes AJ, Bakker SC, van Meir CA, von Lindern J, Boon J, de Boer IP, Rijnders RJ, Jacobs CJ, Uiterwaal CS, Mol BW, Visser GH, van Bel F, Derks JB. Antenatal allopurinol for reduction of birth asphyxia induced brain damage (ALLO-Trial); a randomized double blind placebo controlled multicenter study. BMC Pregnancy and Childbirth 2010;10:8.
<br><br>
Kaandorp JJ, van Bel F, Veen S, Derks JB, Groenendaal F, Rijken M, Roze E, Uniken Venema MMA, Rademaker CMA, Bos AF and Benders MJNL. Long-term neuroprotective effects of allopurinol after moderate perinatal asphyxia. Follow-up of two randomised controlled trials. Arch Dis Child Fetal Neonatal Ed. 2011 Nov 17.