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

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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-...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28692

Bron
Nationaal Trial Register

Verkorte titel
ALLO-trial

Aandoening

perinatal asphyxia, neuroprotection, allopurinol, newborn, oxidative stress

Ondersteuning

Primaire sponsor: Prof dr. F. van Bel
Overige ondersteuning: ZonMW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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).

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

- Prim: immediately at birth

- Sec: 2 years of age

Onderzoeksproduct en/of interventie

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

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Congenital, chromosomal or syndromal malformations.

Onderzoeksopzet

Opzet

Type: Interventie onderzoek

Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-01-2009
Aantal proefpersonen:	220
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	16-07-2008
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 36929
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Register	ID
OMON	NL-OMON36929

Resultaten

Samenvatting resultaten

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.

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.

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

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.

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.