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Neurodevelopmental outcome after neonatal hypoglycaemia: a multi-centre randomised controlled trial comparing intensive treatment versus expectant glucose monitoring in 'high risk' newborns

Submission date 23/08/2007	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 23/08/2007	**Overall study status** Completed	
Last Edited 06/02/2020	**Condition category** Pregnancy and Childbirth	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.studies-obsgyn.nl/hypoexit.nl

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
ZonMW Doelmatigheid 80-007022-98-07406

Study information

Scientific Title
Neurodevelopmental outcome after neonatal hypoglycaemia: a multi-centre randomised controlled trial comparing intensive treatment versus expectant glucose monitoring in 'high risk' newborns

Acronym
HYPO-EXIT

Study objectives
Current clinical practice varies widely, especially for infants with 'moderate' hypoglycaemia, due to lack of methodological sound studies. This leads to both over- and under-treatment of hypoglycaemic infants.

This study-protocol is directed at the comparison of two accepted management strategies at both ends of the current treatment-spectrum of moderate hypoglycaemia in 'high risk' newborns: an intensive treatment versus an expectant monitoring strategy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Multicentre, randomised, single-blinded, active controlled, parallel group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Developmental-disabilities, blood-glucose, hypoglycaemia

Interventions
In the intensive treatment arm the aim is to increase the glucose concentration above 2.5 mmol /l within three hours by increasing the carbohydrate intake by oral nutrition and/or intravenous glucose administration.

In the expectant arm the aim is to maintain the glucose concentration above 2.0 mmol/l by the usual oral nutrition protocol.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Glucose

Primary outcome measure
Primary outcome is neurodevelopment at 18 months, assessed with the Bayley Scales of Infant Development.

Secondary outcome measures
Current secondary outcome measures as of 04/09/2019:
1. Costs for medical treatment and hospital admission until 18 months of age:
1.1 costs for diagnostic tests and treatment of the infant (glucose measurements, supplemental feeding, tube-feeding, intravenous glucose administration), and hospitalization costs for both the infant and mother
1.2 costs for medical consumption related to neurodevelopmental impairment until the age of 18 months (visits to healthcare professionals and hospital admission after the neonatal period)
2. Plasma glucose concentrations and carbohydrate intake (breastfeeding, oral or enteral feeding and intravenous glucose)
3. Frequency of treatment failure, defined as infants who become severely hypoglycaemic despite the treatment they received (frequency and severity of hypoglycaemia episodes after randomization).

Previous secondary outcome measures:
Secondary outcomes are costs for medical treatment and hospital admission until 18 months of age.

Overall study start date
01/10/2007

Completion date
01/04/2013

Eligibility

Key inclusion criteria
Current participant inclusion criteria as 04/09/2019:
Infants greater than or equal to 35 weeks gestational age and greater than or equal to 2000 g with one of the four major risk factors for neonatal hypoglycaemia:
1. Small-for-Gestational-Age infants (SGA, birth-weight-for-gestational-age less than P10)
2. Large-for-Gestational-Age infants (LGA, birth-weight-for-gestational-age greater than P90)
3. Near-term infants 35 0/7 to 36 6/7 weeks gestational age with a birth weight greater than 2000 g
4. Infants of Diabetic Mothers (IDM)
Birth-weight-for-gestational-age is defined according to the growth charts of the Perinatale Registratie Nederland (PRN).

Previous participant inclusion criteria:
Infants greater than or equal to 35 weeks gestational age and greater than or equal to 2000 g with one of the four major risk factors for neonatal hypoglycaemia:
1. Small-for-Gestational-Age infants (SGA, birth-weight-for-gestational-age less than P10)
2. Large-for-Gestational-Age infants (LGA, birth-weight-for-gestational-age greater than P90)
3. Near-term infants 35 0/7 to 36 6/7 weeks gestational age with a birth weight greater than 2000 g
4. Infants of Diabetic Mothers (IDM)
Birth-weight-for-gestational-age is defined according to the Kloosterman growth charts.

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
800

Total final enrolment
689

Key exclusion criteria
Current participant exclusion criteria:
Infants with serious co-morbidity will be excluded, because their co-morbidity can also affect neurodevelopment:
1. Very preterm infants (less than 34 6/7 weeks gestational age)
2. Severe perinatal asphyxia - presence of at least three of the next criteria:
2.1. Signs of intrauterine asphyxia, like late decelerations on Cardiotocogram (CTG) or meconium stained amniotic fluid
2.2. Arterial umbilical cord pH less than 7.10
2.3. Delayed initiation of spontaneous respirations greater than 5 minutes after birth
2.4. Five minute Apgar score less than 5

2.5. Multi-organ failure
3. Severe perinatal infection: requiring support of vital functions (infants without clinical signs of infection who are treated with antibiotics because of suspected perinatal infection can be included)
4. Respiratory insufficiency requiring respiratory support
5. Severe hypotension requiring vasopressor support
6. (Strong suspicion of) a syndrome or major congenital malformations

Other exclusion criteria:
7. Intravenous glucose administration before randomization
8. (Strong suspicion of) inborn error of metabolism
9. (Strong suspicion of) hyperinsulinism, except infants of diabetic mothers
10. No informed consent

Previous participant exclusion criteria:
Infants with serious co-morbidity will be excluded, because their co-morbidity can also affect neurodevelopment:
1. Very preterm infants (less than 34 6/7 weeks gestational age)
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2.5. Multi-organ failure
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Other exclusion criteria:
7. (Strong suspicion of) inborn error of metabolism
8. (Strong suspicion of) hyperinsulinism, except infants of diabetic mothers
9. No informed consent

Date of first enrolment
01/10/2007

Date of final enrolment
01/04/2011

Locations

Countries of recruitment
Netherlands

Study participating centre

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Sponsor information

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Academic Medical Centre (AMC) (The Netherlands)

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Sponsor type
Hospital/treatment centre

Website
http://www.amc.uva.nl/

ROR
https://ror.org/03t4gr691

Funder(s)

Funder type
Research organisation

Funder Name
The Netherlands Organisation for Health Research and Development (ZonMw) (The Netherlands)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	06/02/2020	06/02/2020	Yes	No