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A multicentre randomised controlled trial of low versus high threshold treatment in preterm infants with progressive posthaemorrhagic ventricular dilatation

Submission date
27/01/2006

Recruitment status
No longer recruiting

Registration date
27/01/2006

Overall study status
Completed

Last Edited
25/05/2018

Condition category
Pregnancy and Childbirth

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Babies that are born early (premature) are at increased risk of bleeding into the fluid-filled areas inside the brain (ventricles), called intraventricular haemorrhage, which can lead to enlargement of the ventricles, called posthaemorrhagic ventricular dilatation (PHVD). If the ventricles become larger than a threshold size, about 50 – 60 % of the infants will require surgery to place a tube (shunt) in the brain to drain fluid, about 20 % will not survive, and more than 60 % will be disabled. The aim of this study is to find out whether earlier treatment of PHVD at a lower threshold size decreases the need for shunting and improves patient outcome.

Who can participate?
Premature infants with a gestational age under 34 weeks with intraventricular haemorrhage and PHVD

What does the study involve?
The infants are randomly allocated to the low threshold group or the high threshold group. Those in the low threshold group are treated when the ventricles reach a lower size threshold compared with the high threshold group. Treatment consists of lumbar punctures, where a needle is inserted into the lower part of the spine to drain fluid. If lumbar punctures are still needed over 28 days after the first one, a shunt is inserted into the brain to drain fluid. The two groups are compared with regard to how many infants need a shunt and their brain development at two years of age.

What are the possible benefits and risks of participating?
The low threshold group may benefit from avoiding the need for shunting, but may be at risk of having unnecessary surgery when they may have otherwise stabilized spontaneously.

Where is the study run from?
Wilhelmina Children's Hospital Utrecht and University Medical Centre Utrecht (Netherlands)

When is the study starting and how long is it expected to run for?
January 2006 to January 2014

Who is funding the study?
Sophia Kindergeneeskunde B.V. (Netherlands)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00875758

Secondary identifying numbers
MEC-2005-007; NTR413

Study information

Scientific Title
A multicentre randomised controlled trial of low versus high threshold treatment in preterm infants with progressive posthaemorrhagic ventricular dilatation

Acronym
PHVD

Study objectives
We hypothesise that in preterm infants with a gestational age below 34 weeks a low threshold intervention (progressive posthaemorrhagic ventricular dilatation [PHVD] with a ventricular enlargement above the 97th centile for gestational age according to Levene and a diagonal width enlargement of the frontal horn above 6 mm according to Davies) will decrease the need for a ventriculoperitoneal shunt as compared to high threshold intervention (PHVD exceeding 4 mm over the 97th centile according to Levene and an increase in diagonal width of the frontal horn above 10 mm according to Davies) and will improve neurodevelopmental outcome at two years of age.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Posthaemorrhagic ventricular dilatation

Interventions
Comparison: low threshold versus high threshold intervention.

Low threshold: intervention when an increase in ventricular width according to Levene above the 97th centile towards the P97 + 4 but without crossing the >P97 + 4 and an increase in diagonal width according to Davies above 6 mm towards 10 mm, but not above 10 mm.

High threshold: intervention after an increase in ventricular width according to Levene above the P97 + 4 and an increase in diagonal width according to Davies above 10 mm.
Intervention:

Lumbar punctures (LP; 10 ml/kg) on 2 days. Cranial ultrasound is repeated daily. If on the third day a LP is still required, a subcutaneous reservoir will be inserted. Daily 10 cc/kg will be drained

in 2 taps a day. Punctures from the reservoir will be continued over the next days or weeks. The amount of CSF drained will be increased or decreased in order to reach and keep the ventricular index according to Levene <P97 and diagonal anterior horn width <6 mm. If punctures are still necessary exceeding 28 days after the first LP, a ventriculoperitoneal shunt is inserted. If the bodyweight of the infant is less than 2.5 kg, the insertion of the shunt will be postponed until the bodyweight is over 2.5 kg, if CSF drainage is still needed then.

Intervention Type
Procedure/Surgery

Primary outcome measure
Need for ventriculoperitoneal shunt

Secondary outcome measures
1. Neurodevelopmental outcome on the Bayley Scales of Infant Development at 24 months corrected age, assessed by a blinded developmental psychologist
2. Number of (lumbar) punctures, reservoirs, reservoir dysfunctions, reservoir infections and reservoir revisions, drains, drain dysfunctions, drain infections and drain revisions

Overall study start date
01/01/2006

Completion date
01/01/2014

Eligibility

Key inclusion criteria
Current inclusion criteria as of 03/01//2012
Premature infants with:
1. A gestational age equal to or below 34 weeks
2. An intraventricular haemorrhage grade III according to Volpe (>50% of the ventricle) and grade IV haemorrhage
3. A progressive posthaemorrhagic ventricular enlargement above the 97th centile for gestational age according to Levene and a diagonal width enlargement of the frontal horn above 6 mm according to Davies

Previous inclusion criteria
Premature infants with:
1. A gestational age equal to or below 34 weeks
2. An intraventricular haemorrhage grade III according to Volpe (>50% of the ventricle)
3. A progressive posthaemorrhagic ventricular enlargement above the 97th centile for gestational age according to Levene and a diagonal width enlargement of the frontal horn above 6 mm according to Davies

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
125

Key exclusion criteria
Current exclusion criteria as of 03/01//2012
1. Congenital cerebral malformation
2. Periventricular leucomalacia > grade II according to de Vries
3. Posthaemorrhagic ventricular dilatation already present at birth
4. Central nervous system infection
5. Metabolic disease

Previous exclusion criteria
1. Congenital cerebral malformation
2. Cerebral parenchymal haemorrhage
3. Periventricular leucomalacia > grade II according to de Vries
4. Posthaemorrhagic ventricular dilatation already present at birth
5. Central nervous system infection
6. Metabolic disease

Date of first enrolment
01/01/2006

Date of final enrolment
01/01/2014

Locations

Countries of recruitment
Netherlands

Sweden

United Kingdom

United States of America

Study participating centre
University Medical Centre Utrecht
Utrecht
Netherlands
85090

Sponsor information

Organisation
Erasmus Medical Centre (Netherlands)

Sponsor details
Sophia Children's Hospital
Department Neonatology Intensive Care
Dr. Molewaterplein 60
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Sponsor type
Hospital/treatment centre

Website
http://www.erasmusmc.nl/

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Sophia Kindergeneeskunde B.V. (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	01/01/2019		Yes	No