Brain Injury in Moderate Preterm Neonates

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To assess in moderate preterm infants:1) The prevalence and characteristics of brain injury; 2) The relation between perinatal factors and brain injury;3) The validity of cUS for detection of brain injury as compared to MRI (considered the golden…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neurological disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON41869

Source
ToetsingOnline

Brief title
BIMP

Condition

- Neurological disorders congenital
- Congenital and peripartum neurological conditions

Synonym
Brain injury

Research involving
Human

Sponsors and support

Primary sponsor: Isala Klinieken
Source(s) of monetary or material Support: verzekeraar en ziekenhuis

Intervention

Keyword: Brain damage, Moderate preterm, Neonates

Outcome measures

Primary outcome

Presence/absence of brain injury on cUS at day 3 and/or 7 and/or on cUS and/or

MRI at TEA (composite endpoint of all diagnostic modalities and time points).

Secondary outcome

1. Maternal factors

2. Intra-partum factors

3. Infant factors

4. Presence/absence of brain injury on cUS at day 3

5. Presence/absence of brain injury on cUS at day 7

6. Presence/absence of brain injury on cUS and/or MRI at TEA

7. Presence/absence of abnormal findings at neurological examination at TEA

8. Presence/absence of abnormal neurodevelopmental outcome at 2 years of age

Study description

Background summary

Annually in the Netherlands 14.000 neonates are born prematurely at a gestational age (GA) less than 37 weeks. Very preterm neonates (GA < 32 weeks) are at risk of brain injury, acquired during the perinatal and neonatal period. This is strongly related to neurological impairment, including motor and cognitive deficits, sensorineural hearing loss, cerebral visual impairment and behavioural problems.
The vast majority (80%) of preterm neonates, however, is born moderately prematurely (GA 32-37 weeks). Only since recently it is known that they also have an increased risk for disabilities, as compared to healthy, full term neonates. It may be assumed that these disabilities are related to brain

injury, acquired during the perinatal and/or neonatal period. This has, however, never been investigated: little is known about the prevalence, characteristics and consequences of brain injury in the much larger group of moderate preterm neonates.
Almost all knowledge about preterm brain injury is obtained from extensive research performed in the very preterm population. The disabilities in these children related to perinatal and/or neonatal brain injury are not only a problem for the individual child and its family but, due the immense costs, also for the society. In the Netherlands the estimated annual costs, needed for the care of disabled very preterm children is about ¤11.000.000. This excludes the much higher institutional costs. Since many decennia medical care for very preterm neonates is highly centralized: immediately after birth these vulnerable infants are admitted to a Neonatal Intensive Care Unit (NICU) and undergo highly specialized medical and nursing care. To enable early detection of brain injury, very preterm infants undergo neuro-imaging, consisting of serial cranial ultrasound (cUS) examinations from birth until term equivalent age (TEA) and in many cases also an MRI-examination around TEA. In addition, after discharge, they undergo standardized follow-up programs, enabling early diagnosis of neurological impairment and thus early interventions (such as physiotherapy, speech therapy, hearing aid, physical rehabilitation, visual rehabilitation). In very preterm neonates these early interventions are successful for prevention of (serious) disabilities and improving functional outcome.
The much larger group of moderate preterm infants is also at risk of disabilities and abnormal neurological development. They have a 2-fold higher prevalence of developmental delay, more problems with fine motor skills, communication, and personal-social functioning at preschool age, and more grade retention and need for special educational at school age than full term children. In adulthood they perform less.
In contrast to very preterm infants, moderate preterm infants are not admitted to a NICU, but to neonatal wards of general hospitals. They receive far less specialized care and do not routinely undergo neuro-imaging examinations or standard follow-up programs.
As the group of moderate preterm children is so much larger than the group of very preterm children, the economic and social consequences of even a slightly increased risk of abnormal outcome are probably much larger than for the very preterm group. Knowledge about perinatal/neonatal brain injury and its consequences is essential for prevention and treatment strategies. This may lead to better functional outcomes and thus significant reduction of health care costs.

Study objective

To assess in moderate preterm infants:
1) The prevalence and characteristics of brain injury;
2) The relation between perinatal factors and brain injury;
3) The validity of cUS for detection of brain injury as compared to MRI

(considered the golden standard);
4) The relation between neurological examination at TEA and brain injury;
5) The relation between neurodevelopmental outcome at 2 years of age and brain injury.

Study design

A prospective, longitudinal observational neuro-imaging study.

Study burden and risks

There is no risk associated with study participation.
The neuro-imaging techniques we will apply are safe and non-invasive and the neonatal team has ample experience with both techniques. cUS is performed at the bedside with little disturbance to the infant. It has routinely been used worldwide since the early eighties to detect brain injury in very preterm and other high-risk neonates. It is safe and reliable for the detection of many forms of neonatal brain injury.
MR imaging of the brain has been applied in many NICUs since the nineties for more precise and reliable detection of brain anomalies in high-risk neonatal populations. It gives detailed and additional information on the exact site and extent of lesions and on brain maturation. It therefore further helps to prognosticate. MRI is biologically harmless. No short- or long-term adverse effects from MRI at field strengths and durations clinically used have been identified to date. MRI will be performed at TEA during natural sleep, shortly after a feed. We will bundle the infants prior to the MRI examinations and will not apply sedation. Ear protection, specially designed for neonatal MRI at 3-Tesla field strength will be provided. Infants will be guided through the whole procedure, including transportation to and from the MR department by a neonatologist or nurse-practioner experienced in neonatal MRI procedures and neonatal resuscitation. All standard safety precautions, including MRI compatible monitoring of heart rate and oxygen saturation for neonatal MRI will be followed.There is a small burden related to the MRI procedure, as the infants need to be admitted for * day.
Participation in this study may lead to early detection of major brain abnormalities. We will not inform parents on the brain imaging findings, with the exception of parents of infants with major brain abnormalities that will likely have severe consequences for outcome (such as cerebral palsy and severe cognitive impairment) and for which early interventions are likely to improve outcome. As early interventions can thus be initiated, this may be beneficial for the individual child.
If a higher prevalence of brain injury is found in moderately preterm neonates as compared to full term neonates38-44, screening for brain injury is indicated in this patient group. This will lead to early detection of brain abnormality.
On the long term the study may therefore contribute to better health of moderate preterm children and may thus be beneficial for this specific group

and the society

Contacts

Public
Isala Klinieken

Dokter van Deenweg 2
Zwolle 8025 BP
NL
Scientific
Isala Klinieken

Dokter van Deenweg 2
Zwolle 8025 BP
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Born prematurely, gestational age 32-36 weeks;
2. Admission to the neonatal high care or medium care unit.

Exclusion criteria

1. Congenital malformations of the central nervous system;
2. Chromosomal disorders;
3. Inborn errors of metabolism;

4. Congenital infections;
5. Central nervous system infections;
6. Brain injury acquired after the neonatal period
7. Parents do not speak Dutch or English

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-08-2017
Enrollment:	254
Type:	Actual

Ethics review

Approved WMO Date:	26-10-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-02-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-06-2017
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-08-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-07-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-10-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-02-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-12-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
CCMO	NL52323.075.15