Cerebral perfusion during neonatal cardiac surgery: Can we improve outcome?

Published: 11-11-2008
Last updated: 11-05-2024

In a randomized controlled trial, the effects of DHCA and ACP during complex neonatal cardiac surgery on organ function and injury will be compared, especially focusing on cerebral damage and neurological outcome. The primary research question is...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON35580

Source
ToetsingOnline

Brief title
Immunological and cerebral effects of neonatal cardiac surgery

Condition

- Immune disorders NEC
- Neurological disorders NEC
- Cardiac therapeutic procedures

Synonym
aortic arch reconstructions, congenital heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Brain injury and development, Cardiopulmonary Bypass, Inflammation, organ failure

Outcome measures

Primary outcome

Percentage of infants with new or worsened lesions on the postoperative MRI

(compared to the preoperative MRI-scan).

Secondary outcome

- Cerebral damage:

o Serum markers: Average of S100beta 4, 24 hours and 1 week postoperatively

o aEEG monitoring: The average duration postoperatively, after which the aEEG

returns to a normal pattern

o NIRS: The average postoperative duration of NIRS-values < 45%

o Neurological abnormalities: Percentage of infants with neurological

abnormalities within 72 hours postoperatively

o Neurodevelopmental outcome: Percentage of infants with a neurodevelopmental

delay at 9 months

- Organ failure:

o Mortality (within 30 days and during follow-up)

o Multi-organ failure: Percentage of infants with multi-organ failure during

hospital stay, using the *modified SOFA- score* (Shime et al.)

o Serum markers: Average of serum markers 4, 24 hours and 1 week

postoperatively

- Inflammation:

o Average cytokine levels 4, 24 hours and 1 week postoperatively, both in the brain and systemically

o Percentage of activated and regulatory T-cells and monocytes 24 hours and 1 week after surgery

Study description

Background summary

Neonates with a congenital heart defect (CHD) often need to undergo early cardiac surgery. In complex heart defects, cardiopulmonary bypass (CPB) is usually employed, with or without deep hypothermic circulatory arrest (DHCA). During this procedure two main mechanisms are thought to induce a systemic inflammatory response syndrome (SIRS). These are the ischemic-reperfusion injury and the contact of blood with foreign material. An imbalance in both the innate and adaptive immune system is thought to cause the inflammatory response which subsequently occurs. It can lead to a state of systemic inflammation, endothelial damage and, ultimately, to multi-organ failure.

The brain is especially vulnerable to ischemic injury, which puts neonates undergoing complex operations at high risk of neurodevelopmental disorders. Selective antegrade cerebral perfusion (ACP) instead of DHCA during these complex operations may contribute to less brain injury, but research performed has not been conclusive on this issue.

Study objective

In a randomized controlled trial, the effects of DHCA and ACP during complex neonatal cardiac surgery on organ function and injury will be compared, especially focusing on cerebral damage and neurological outcome.

The primary research question is whether ACP reduces cerebral damage compared to DHCA, as assessed by MRI-lesions. Secondary research questions focus on the effects of ACP and DHCA on inflammatory response, endothelial damage and organ

failure.

Study design

In a randomized controlled trial 30-50 infants (age < 4 months), undergoing aortic arch reconstruction, will undergo surgery using either DHCA or ACP. The primary outcome will be the rate of new or worsened MRI-lesions postoperatively, compared to pre-operative MRI- scans. Secondary outcomes will be cerebral damage, organ failure and inflammation. Cerebral damage will be measured by serum cerebral damage markers, aEEG, NIRS, acute neurological abnormalities and adverse neurodevelopmental outcome (until 9 months after the operation). Organ failure will be measured serum organ injury markers, clinical organ failure and mortality. Inflammation will be measured by cytokine and activated T-cell and monocyte levels.

The results of this study will be the basis for a long term follow-up study on DHCA and ACP.

Intervention

One group will receive DHCA and the other group will receive ACP.

Study burden and risks

The neonates will be randomly assigned to either DHCA or ACP. Currently, worldwide, both perfusion techniques are used. In our hospital both techniques are used in a standardized way. Therefore, there is no specific burden or risk of the application of either perfusion techniques. Blood will be drawn in accordance to the hemodynamic stability of the infant and is safe as demonstrated in previous studies on neonates by our research group (METC 03/039, 04/144, 05/041). The cerebral monitoring used is already part of the standard of care at our department. MRI scans are known to be a safe imaging technique, and will be performed under direct supervision of a pediatric cardiac anesthesiologist. MRI*s are often already performed perioperatively and is a standard in asphyxiated neonates.

The greatest burden, is the time consumption of this study for the child and his/ her parents during the follow-up after the operation at the out-patient clinic (two check-ups of 45 minutes each during the first year of life).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Infants (<4 months of age) that will undergo an aortic arch reconstruction

Exclusion criteria

Children that:
- have objective evidence of infection
- have failed to have tissue or laboratory data collected
- participate in another clinical trial
- have an expected longer duration of aortic arch reconstruction than 60 minutes
- need to be sedated and intubated especially for the pre-operative MRI scan of this research project

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-02-2009
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	11-11-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	04-01-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL20610.041.08