Fibrinogen therapy for massive blood loss during elective surgery for craniosynostosis repair, a double blinded randomized controlled study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON41510

Source
ToetsingOnline

Brief title
Fibrinogen therapy for massive blood loss in children

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Nervous system, skull and spine therapeutic procedures

Synonym
massive blood loss in fused bones of the skull, massive blood loss in surgery for premature fusion of cranial sutures

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: CSL-Behring,NutsOHRA

Intervention

Keyword: children, fibrinogen therapy, massive blood loss, thromboelastography

Outcome measures

Primary outcome

The purpose is to evaluate the efficacy of fibrinogen therapy at the start of surgery for craniosynostosis repair to reduce the amount of blood product transfusions in ml required. We hypothesize that the blood loss can be significantly reduced by maintaining the level of fibrinogen above 2 g/L. Fewer transfusions will not only reduce the number of blood donors transfused to the patient, but also the potentially acute and long-term side effects and the costs of the transfused blood products.

Secondary outcome

Secondary outcome measures are related to intra- and postoperative blood loss, operation time, stay on the intensive care unit, total hospital stay, and postoperative complications such as thromboembolic events or wound infections. Data of the thromboelastographic monitoring will be correlated to the two study arms.

Study description

Background summary

The management of massive blood loss in children during multiple trauma or

major surgery is still an unsolved problem. No clear strategies and no evidence-based treatment protocols exist.
Primary non-syndromic craniosynostosis occurs in 1:2000 births. Primary operative repair of craniosynostosis in infants and young children is recommended. Unfortunately, this procedure can lead to excessive blood loss and is associated with an average loss of 60 to 100 % (!) of the estimated blood volume. Our institution (Prof Dr L. van Adrichem) performs more than 100 of these craniofacial surgeries per year. These well-planned operations in a homogenous group of young children are a model for excessive acute blood loss especially in children

In a recent prospective pilot study (METC 2008-321) we could prove that monitoring of massive blood loss in children during surgical repair of craniosynostosis with thromboelastography provided evidence for a remarkable dilution coagulopathy. The application of different intraoperative strategies and early interventions have reduced the amount of transfused blood products in adults. Intra-operative monitoring with thromboelastography was helpful in decision making. No studies have evaluated this in children.

Study objective

Primary outcome parameter is the amount of intra- and postoperative transfusions required.

Secondary outcome parameters include intra- and postoperative blood loss, operation time, and postoperative complications and the outcome of thromboelastographic monitoring

Study design

Single-center, randomized, controlled double-blinded trial comparing the efficacy of fibrinogen intervention versus placebo during massive blood loss in children. In order to study the effects of massive blood loss on the coagulation system in otherwise healthy children we selected the primary operative repair of craniosynostosis.

Intervention

The intervention being studied is the application of fibrinogen concentrate (=50 ml) given IV in an individually targeted dose dependent on the preoperative individual plasma fibrinogen level immediately at the start of surgery (in order to reach a level of 3 g/l plasma fibrinogen), followed by 60 mg/kg BW in a continuous infusion during the next hour in the experimental group versus 50 ml of a placebo solution of NaCl 0.9% in the control group at the start of surgery followed by a continuous infusion during the next hour. Repeated TEG measurements will be obtained during surgery, and additional

coagulation tests will be performed to monitor the effect of the intervention.

Study burden and risks

The intervention takes place during the operative procedure by the surgical team of Prof L van Adrichem (plastic surgeon) and Mrs Dr van Veelen (neurosurgeon). Treatment with fibrinogen or with the placebo NaCL 0.9% at the start of surgery will be performed within the protocol for craniosynostosis surgery. According to this protocol standardized blood sampling is done during and after surgery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- children primary non-syndromic craniosynostosis undergoing elective surgical repair. Patients with Muencke syndrome and patients with Saethe-Chotze syndrome however, are eligible.
- written informed consent
- age older than 5 months and younger than 25 months

Exclusion criteria

Exclusion criteria
- coagulation disorders
- hypersensitivity against Haemocomplettan P®
- the presence of a craniofacial malformation syndrome
- anemia
- prior thrombosis

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-09-2012
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Haemocomplettan® P
Generic name:	human fibrinogen
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	20-12-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-07-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EudraCT	EUCTR2011-002287-24-NL
CCMO	NL37008.078.11
Other	NTR nr 10140