TEG based application of fibrinogen in children.

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Fibrinogen therapy at the start of surgery for craniosynostosis repair may reduce the amount of blood product transfusions required.

Ethische beoordeling	Niet van toepassing
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28896

Bron
Nationaal Trial Register

Verkorte titel
RCT TEG: randomized controlled trial for thromboelastography

Aandoening

blood loss
fibrinogen
double-blind trial
craniosynostosis

Ondersteuning

Primaire sponsor: Erasmus MC
Dr. Molewaterplein 60
3015 GJ Rotterdam
the Netherlands
Overige ondersteuning: Sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Perioperative blood loss.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:

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. However, 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 (thromboelastography (TEG) is a clinical monitoring method which monitores the effects of blood loss on blood coagulation) provided evidence for a remarkable dilution coagulopathy. Intra-operative monitoring with TEG, the application of different intraoperative strategies and early interventions will has reduced the amount of transfused blood products in adults. No studies have evaluated this in children.

Objective:

The primary objective is to reduce the perioperative blood loss measured as a reduction in the amount of infused red blood cells with 30%, in children undergoing elective craniosynostosis surgery, using fibrinogen infusion at the start of the operative procedure compared to a placebo-control arm.

Secondary outcome parameters include changes in coagulation parameters, difference in operation time, and postoperative complications between the experimental and the placebo arm.

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.

Study population:

This trial will be performed in children who are undergoing massive blood loss due to a standard operation procedure, and will include children diagnosed with non-syndromic craniosynostosis. These children are undergoing elective surgery when they are aged 8-14 months and have a bodyweight of 8-10 kg. Elective craniofacial repair is performed at the Sophia Children's Hospital, Erasmus MC, Rotterdam.

Intervention:

The intervention being studied is the application of 100 mg/kg BW of fibrinogen concentrate (=50 ml) given IV in a dose of 50 mg/kg body weight (BW) immediately at the start of surgery, followed by 50 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, which is performed according to a standard surgical procedure. Repeated TEG measurements will be obtained during surgery, and additional coagulation tests will be performed to monitor the effect of the intervention.

Main study parameters/endpoints:

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 required. In a pilot study on 47 healthy children undergoing surgical repair of craniosynostosis in 2009 (METC 2008-321) mean blood loss was 79 ml • kg –1 • body weight. We hypothesize that the mean blood loss of 79 ml • kg –1 • body weight can be significantly reduced by maintaining the level of fibrinogen above 2 g/L. A reduction of 30 % of transfusion volume will lessen the mean transfusion volume of 396 ml to 262 ml. That is approximately the volume of one unit packed red blood cell (pRBC). This will decrease significantly the number of blood donors the child will be exposed to.

A sample size of 60 children in each arm will have 80% power to detect a significant difference of 30% in mean transfused blood volume in ml. Thus the total number of patients which need to be randomized is 120. 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.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

This study group serves as a model for excessive acute blood loss in children. To our knowledge there will be no risks associated with the participation to this study. Allergic

reactions to treatment with exogenous fibrinogen concentrate are described with a very low probability and we consider this risk as negligible. Plasma levels of 2-4 g/L are not associated with a higher risk of thrombosis in children. In physiological stress situations like trauma or serious infections, fibrinogen acts as an acute phase protein and will than reach levels above 5 g/L without any clinical problems. Thus we do not expect complications from the intervention with fibrinogen concentrate in these children. The anaesthetic management, fluid replacement and transfusion of blood components will be done according to the standardized local protocol. All children will receive a blinded intervention of either active drug or placebo. During at least 6 fixed moments 3 ml of extra blood will be taken from an in-situ infusion line for additional TEG monitoring. No extra punctures are necessary, no extra visits to the hospital or questions to the parents or guardians are planned.

Doel van het onderzoek

Fibrinogen therapy at the start of surgery for craniosynostosis repair may reduce the amount of blood product transfusions required.

Onderzoeksopzet

Total on study time will be 72 hours from start of surgery or longer when applicable.

An interim analysis will be performed after 20 patients in each arm has been treated to assess safety.

Onderzoeksproduct en/of interventie

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Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Primary non-syndromic craniosynostosis undergoing elective repair from September 2011;

2. Written informed consent;

3. Age older than 5 months and younger than 15 months.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. The presence of congenital bleeding diathesis or congenital prothrombotic risk factors like proteine C or S deficiency or antithrombin deficiency. (Congenital Factor F Leiden and the prothrombin F II mutation are no contraindication for surgery);

2. Known hypersensitivity against Haemocomplettan P®;

3. Known coagulopathy;

4. Presence of a craniofacial malformation syndrome;

5. Active infectious disease;

6. Patients with anemia or thrombocytopenia before the surgical intervention;

7. Patients with prior thrombo-embolic disease.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-09-2011
Aantal proefpersonen:	114
Type:	Werkelijke startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2834
NTR-old	NTR2975
Ander register	Erasmus MC // EudraCT : 201105-RCTTEG // 2011-002287-24
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A