Coagulation monitoring to prevent hemostatic complications in kids on extracorporeal membrane oxygenation

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

Summary

ID

NL-OMON52557

Source
ToetsingOnline

Brief title
CHECKID

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Cardiac disorders, signs and symptoms NEC
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
coagulation in children on heart-lung machine

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum

Source(s) of monetary or material Support: Vrienden van het Sophia

Intervention

Keyword: acquired von Willebrand disease, coagulation test, extracorporeal membrane oxygenation, pediatric

Outcome measures

Primary outcome

1. The first bleeding complication or the first clotting complication in the

first 14 days of ECMO therapy

2. Test results of coagulation tests including ACT, APTT, PT, anti-Xa,

fibrinogen, D-dimer, platelets, VWF act, VWF ag, VWF-CB, VWF multimers, ROTEM

(time to clot initiation: clotting time [CT] in EXTEM and INTEM; clot strength:

maximum clot firmness [MCF] in EXTEM and INTEM; fibrinogen activity: MCF in

FIBTEM; and heparin effect: CT in HEPTEM and INTEM); fibrinolysis (LY 30 in

EXTEM and INTEM), TEG (R in EXTEM and INTEM; MA in EXTEM and INTEM; MA in

FIBTEM; R in HEPTEM and INTEM; CL30 in EXTEM and INTEM), and TGA (ETP).

Secondary outcome

1. Test results of coagulation tests over time during the first 14 days of ECMO

therapy

2. The total number of bleeding and clotting complications in the first 14 days

of ECMO

3. Survival of children with and without hemostatic complications during ECMO

in the first 14 days of ECMO

Study description

Background summary

Extracorporeal membrane oxygenation (ECMO) ECMO has become increasingly important as supportive therapy for patients with life-threatening cardiac and/or respiratory failure. Despite improvement in technology and increasing clinical practice, the incidence of hemostatic complications remain high and they are the primary causes of morbidity and mortality in patients treated with ECMO worldwide. Bleeding and clotting complications occur in about 50% of the pediatric ECMO patients, associated to a decrease in survival of about 40%. The interaction between blood and the ECMO circuit generates a hypercoagulable state, and unfractionated heparin is used to maintain patency of the circuit as well as to reduce thrombotic events while minimizing bleedings. Worldwide, no consensus exists about how to monitor this precarious hemostatic balance. Current conventional tests (APTT, ACT, anti-FXa assay, platelets, d-dimer, fibrinogen, antithrombin) assess only isolated parts of the coagulation cascade, while alternative tests (TEG/ROTEM and TGA) assess the complete coagulation cascade. In addition, acquired von Willebrand disease (AVWD) may add to the bleeding problems in ECMO patients. The incidence and association with bleeding complications in pediatric ECMO patients, however, is unknown. We hypothese that the alternative coagulation tests better reflect the thrombotic or haemorrhagic phenotype than the conventional tests, and as a consequence will improve coagulation monitoring in ECMO patients, leading to less hemostatic complications and improved survival. Furthermore, we hypothese that AVWD contributes to the bleeding problems in children on ECMO.

Study objective

The primary objectives of this study are:
1. to investigate the association between both conventional and alternative coagulation tests, and hemostatic complications, including bleeding and clotting complications in pediatric ECMO patients
2. to investigate the incidence and severity of AVWD and its association with bleeding complications in pediatric ECMO patients

The secondary objectives of this study are :
1. to analyze the longitudinal hemostatic profile over time in ECMO children
2. to analyze the incidence of bleeding and clotting complications during the first 14 days of ECMO therapy
3. to analyze the mortality associated with hemostatic complications during the first 14 days of ECMO therapy
4. to analyze the longitudinal presence and severity of AVWD over time in ECMO children

Study design

This is a prospective, multicenter, observational study of pediatric patients (0-17 years old) on ECMO in the centers of the Phoenix consortium during three years.

The Pediatric HematOlogy Extracorporeal circulation NetworX (PHOENiX) consortium consists of ECMO centers of Rome (Bambino Gesù Hospital, Dr A Rizza), London (Great Ormond Street, Dr A Hoskote, Dr A Karimova), Detroit (Children*s Hospital of Michigan, Dr M Chitlur), Toronto (SickKids, Dr L Brandao), Edmonton (Stollery Children*s Hospital, Prof. P. Massicotte), Nijmegen (Radboudumc, Dr. A. van Heijst), Vienna (University Children*s Hospital, Prof. C. Male) and Rotterdam (Sophia Children*s Hospital ErasmusMC, Dr CH van Ommen, Dr E Wildschut).

Study burden and risks

Hemostatic complications, including bleeding and thrombotic complications, occur in about 50% of the pediatric patients on ECMO. Death is associated with these complications in more than one third of these patients. Therefore, prevention of these complications is rather important. This study investigates the association between conventional and/or alternative coagulation tests and the hemostatic complications and the incidence of AVWD and its association with bleeding in children on ECMO.
If one or a combination of the coagulation tests appear to have a good association with hemostatic complications, the test(s) can be incorporated in a new anticoagulation protocol, that might cause less hemostatic complications and thus decreases mortality in this patient group. In addition, if AVWD may cause bleeding in ECMO patients, treatment of AVWD, for example with VWF concentrate, may be a prophylactic or treatment option.

The risk of this study is extra blood withdrawal. The extra blood needed varies between 2.0 mL and 4.5 mL/day depending on age and the type of tests performed on routine base. (TGA and VWF is always extra, ROTEM in some centers). Blood will always be taken from a central line or ECMO circuit. It may be possible that patients need a red cell transfusion earlier due to the withdrawal of blood. Benefit: patients will be checked very thoroughly on hemostatic complications due to the study and diagnosis of these complications may be made earlier.

It is important to perform this study in pediatric patients as the hemostatic system develops over time from neonatal to adult age. Although all components of the hemostatic system are present at birth, important differences exist among preterm and term neonates, older children and adults. This is called *developmental hemostasis*. These differences have important consequences for interpretation of laboratory results during ECMO among others. It is therefore

not possible to extrapolate from adult results.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

Children from 0 to 17 years old treated on ECMO in the participating ECMO centers can be included in this study.

Exclusion criteria

1. Patients without informed consent
2. Patients after 24 hours of start of ECMO

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-09-2019
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	03-07-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-02-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-07-2020

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-07-2022
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

ID: 28010
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL66711.078.18
OMON	NL-OMON28010