Safety and efficacy of nadroparin in neonates: an observational study.

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Therapeutic nadroparin administration:Primary objective: To develop evidence-based dosing regimens of nadroparin for extremely premature, premature and term neonates by means of the objectification of the PK/PD of nadroparin.Secondary objective: 1)...

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

Summary

ID

NL-OMON56793

Source
ToetsingOnline

Brief title
SAFE-NEO

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Neonatal and perinatal conditions

Synonym
blood cloth, Thrombosis

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Trombosestichting Nederland

Intervention

Keyword: Bleeding, efficacy, nadroparin, neonates

Outcome measures

Primary outcome

Therapeutic nadroparin administration:

To establish evidence-based therapeutic dosing regimens of nadroparin for extremely premature, premature and term neonates by means of objectification of the PK/PD of nadroparin during standard care.

Prophylactic nadroparin administration:

To establish evidence-based therapeutic dosing regimens of nadroparin for premature and term neonates by means of objectification of the PK/PD of nadroparin during standard care.

premature and term neonates

Secondary outcome

Therapeutic nadroparin administration:

Secondary endpoint:

1. The incidence of complete thrombus resolution in relation to anti Xa levels within 3 months after the start of nadroparin treatment

2. The incidence of major, clinically relevant and minor bleeding and its relation to anti Xa levels during treatment with nadroparin until 24 hours after termination of nadroparin

Prophylactic nadroparin administration:

Secondary endpoint:

1. The incidence of new or recurrent thrombosis in relation to anti Xa levels

during treatment with nadroparin

2. The incidence of major, clinically relevant and minor bleeding and its

relation to anti Xa levels during treatment with nadroparin until 24 hours

after termination of nadroparin

Study description

Background summary

The incidence of venous thrombosis is rising rapidly in neonates.[1,2] This rise is the result of improved neonatal care over the past 20 years resulting in an increase in the survival of (extremely) premature and critically ill infants. When a venous thrombus occurs there is an indication for therapeutic anticoagulant treatment (anti Xa levels 0.5-1.0 IU/mL). Inhibition of the coagulation system gives the opportunity to resolve the clot. If neonates are at high risk for venous thrombosis preventive measures can be taken by prophylactic anticoagulant treatment (anti-Xa levels 0.1-0.4 IU/mL). This inhibits the coagulation system in a lesser way compared to therapeutic anticoagulant treatment and prevents formation of a thrombus.
In the Netherlands each year 250 neonates receive off-label therapeutic and prophylactic nadroparin treatment, without any information on the pharmacokinetics/-dynamics (PK/PD) and therefore optimal and safe dosage regimen. As a result, these neonates are prone to suboptimal treatment with a risk for thrombosis, a lack of thrombus resolution or major bleeding.
Therefore we designed an observational study during standard care to objectify the PK/PD in neonates.

Study objective

Therapeutic nadroparin administration:
Primary objective:
To develop evidence-based dosing regimens of nadroparin for extremely premature, premature and term neonates by means of the objectification of the PK/PD of nadroparin.
Secondary objective:

1) Investigate the relation between anti Xa levels and thrombus resolution within 3 months after the start of nadroparin treatment
Investigate the relation between anti Xa levels and bleeding during treatment with nadroparin until 24 hours after termination of nadroparin
Prophylactic nadroparin administration:
Primary objective:
To develop evidence-based dosing regimens of nadroparin for premature and term neonates by means of the objectification of the PK/PD of nadroparin.
Secondary objective:
1) Investigate the relation between anti Xa levels and new or recurrent thrombosis during treatment with nadroparin

Study design

A national observational prospective study, conducted in 6 Neonatal Intensive Care Units/ Children*s Hospitals in the Netherlands.

Study burden and risks

As mentioned above, each year 250 neonates receive off label nadroparin treatment without any information on PK/PD and therefore optimal and safe therapeutic or prophylactic dosage regimen. Despite this off label treatment, dosage recommendations have been provided. As a result, these neonates are prone to suboptimal treatment with a risk of a new thrombosis, a lack of thrombus resolution, or major bleeding. This bleeding has an impact on the morbidity and survival of neonates Therefore we will perform an observational study during standard care to objectify the PK/PD in neonates. With the development of evidence-based therapeutic dosing regimens for extremely premature, premature and term neonates, and evidence-based prophylactic dosing regimens for premature and term neonates for nadroparin we can ensure these vulnerable neonates an effective treatment without toxicity, and therefore less complications. A possible risk is reducing the circulating blood volume of neonates by taking blood. Therefore we minimized the volume blood samples (5 mL in total per neonate). To avoid the burden of venepunctures we aim to include mainly neonates with central venous or arterial access and combine blood samples with standard blood samples.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Newborns
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

Neonates already receiving therapeutic or prophylactic nadroparin dosage as part of their treatment.

Exclusion criteria

•No informed consent
•Major congenital malformations
•Metabolic disorders
•Previous cerebral bleeding
•Neonates with any condition that, as judged by the investigator, would place the neonate at increased risk of harm if he/she participated in the study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2024
Enrollment:	75
Type:	Anticipated

Ethics review

Approved WMO

Date:	24-05-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL84834.018.24