Pentoxifylline dose optimization in preterm neonatal sepsis

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Ethical review	Approved WMO
Status	Completed
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON49542

Source
ToetsingOnline

Brief title
Pentoxifylline in neonatal sepsis

Condition

- Bacterial infectious disorders

Synonym
bloodstream infection, late onset sepsis (LOS)

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Zon Mw

Intervention

Keyword: dose optimization, pentoxifylline, preterm infant, sepsis treatment

Outcome measures

Primary outcome

Dose optimisation will be based on the clinical and biochemical (CRP, IL-6, PCT, TNF-a) response after 3 days in comparison to baseline and on adverse drug effects.

Secondary outcome

Secondary study parameters include the evaluation of longitudinally determined 91 inflammatory markers (Olink proteomics) and metabolomics of the whole inflammatory panel, to further understand the inflammatory and immunological changes of preterm infants during sepsis with PTX treatment and the pharmacokinetics of PTX and its metabolites in preterm infants. A target concentration of PTX and its metabolites will be calculated and PK/PD model for PTX will be developed.

Study description

Background summary

Sepsis is a very important cause of death in preterm infants. Survival from sepsis is often related to severe short and long term morbidity. Despite optimal antibiotic treatment, immaturity of the immune system in preterm neonates causes this severe sepsis related mortality and morbidity. There is strong indications that preterm neonates with sepsis could benefit, next to antibiotics, from treatment with pentoxifylline (PTX). PTX which is registered for adults with intermittent claudication, is already used in preterm neonates with sepsis. Knowledge about optimal dosing is however limited.

Study objective

The main objective is to determine in what optimal dose PTX should be used in preterm infants suffering from sepsis. Previous clinical studies have already indicated the safety of the drug in preterm infants.

Study design

Dose optimisation study in preterm born infants with late onset sepsis and increased inflammation. In this study different dosages will be evaluated, with dosage step-up and step-down in every 3 patients. Starting dose will be the dose as described in all previous studies. We expect that around 30 included infants are needed to determine the optimal dose using this study design. Subsequently, we will validate this optimal dose in 10 preterm neonates

Intervention

The intervention consists of intravenously administered pentoxifylline (PTX).

Study burden and risks

PTX is already used at our NICU for patients with sepsis, but data on the dose/response curve do not exist. PTX has already been shown to have beneficial effects in humans and animal models of sepsis, especially in preterm infants. A meta-analysis showed that PTX increases the survival of preterm infants suffering from sepsis and suggests that PTX is well tolerated. No severe side effects have been detected in previous studies or in clinical practice of preterm infants .We do expect a therapeutic gain for participants of the study because of the expected benefits from optimized PTX treatment. Improved outcome of neonatal sepsis is expected. During the study a limited amount of additional blood will be collected either from arterial lines or during routine blood drawing. No extra heelsticks or venipunctures will be performed for the study. A maximum amount of 3% of the total blood volume is used for research purposes in a 4 weeks period. Urine will be collected non-invasively. No further additional burden is expected.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Neonates with gestational age <30 weeks
- suspected of late onset sepsis with blood drawn for blood culture and inflammatory biomarkers
- IL-6 > 500 pg/ml and/or CRP > 50 mg/L

Exclusion criteria

- PTX therapy cannot be started within 24 hours of start of antibiotic treatment.
- Patients with known major congenital defects (e.g. congenital heart disease, pulmonary, or gastrointestinal anomalies) will also be excluded.
- If subjects have IL-6 values exceeding 25000 pg/mL at time of onset they will also be excluded. High IL-6 values represent severe episodes of sepsis and high IL-6 values are associated with high mortality rates.
- Patients who already participated in this trial during an earlier episode of late onset sepsis.
- Patients with pH below 7 in two consecutive blood samples, with at least 1 hour between the blood samples, at start of sepsis episode.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-01-2020
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Trental
Generic name:	Pentoxifylline
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	30-07-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-12-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-03-2021
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	EUCTR2019-002020-33-NL
Other	EudraCT nummer 2019-002020-33
CCMO	NL70075.078.19