Presepsin to safely reduce antibiotics in preterm infants (PRESAFE trial): a randomized controlled trial with concurrent observational cohort

Published: 25-06-2024
Last updated: 27-12-2024

To investigate whether addition of a presepsin-guided step to the Dutch EOS guideline safely reduces unnecessary empirical antibiotic exposure directly after birth in preterm infants born

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

Summary

ID

NL-OMON56856

Source
ToetsingOnline

Brief title
PRESAFE trial

Condition

- Bacterial infectious disorders

Synonym
blood stream infection, early-onset sepsis

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: ZonMW subsidie "Goed Gebruik

Geneesmiddelen"

Intervention

Keyword: antibiotics, biomarker, preterm infants, sepsis

Outcome measures

Primary outcome

In all patients <32 weeks of gestation presepsin levels will be determined in plasma preferably derived from umbilical cord blood. The co-primary outcomes of the RCT are: 1) the incidence of a culture-proven EOS (non-inferiority) and 2) unnecessary antibiotics administration (superiority). The primary outcome of the observational part is the diagnostic accuracy of presepsin directly after birth for EOS.

Secondary outcome

Secondary outcomes include: sepsis-related severity of illness, total number of antibiotic days (started <72 hours after birth), incidence of the composite outcome of necrotizing enterocolitis, late-onset sepsis, or death, incidence of bronchopulmonary dysplasia, intraventricular haemorrhage and/or periventricular leukomalacia, retinopathy of prematurity. We further will evaluate the neurocognitive outcome and related health care costs.

Study description

Background summary

Accurate and rapid diagnosis of early-onset neonatal sepsis (EOS) remains problematic in preterm infants mainly due to the non-specific signs and symptoms, and lack of reliable, rapid diagnostic tools. Over 80% of preterm infants are empirically started on antibiotics directly after birth, while the

actual incidence of EOS varies between 1-2%. Unnecessary antibiotic exposure leads to severe short term and long term complications. Presepsin is a promising biomarker for reducing antibiotic exposure in preterm infants as concentrations increase rapidly after infection onset and it has a high specificity for bacterial infections.

Study objective

To investigate whether addition of a presepsin-guided step to the Dutch EOS guideline safely reduces unnecessary empirical antibiotic exposure directly after birth in preterm infants born <32 weeks gestation at moderate risk of EOS. Secondly, the diagnostic accuracy of presepsin for EOS will be evaluated.

Study design

Multicenter, parallel groups, superiority and non-inferiority randomized clinical trial (RCT) with a concurrent observational cohort.

Intervention

Intervention: empirical antibiotics will be started when the presepsin level is >645 pg/ml. Comparator: standard care according to the Dutch guideline.

Study burden and risks

Participation in the study involves no additional punctures in the patients, as the biomarker blood sample will be drawn from the umbilical cord or during a regular blood draw within the first 4 hours after birth. Patients at low or high risk of EOS are excluded from the RCT to reduce the extra risk for antibiotic exposure in the low risk group and to reduce the risk for missing EOS cases in the high risk group. For the included patients (who are at moderate risk of EOS, and clinical equipoise is suggested for antibiotic treatment versus no treatment), the hypothetical risk of developing sepsis while not receiving antibiotics is covered by choosing a cut-off value of presepsin with 100% sensitivity. Furthermore, all patients will be closely monitored in an intensive care setting allowing clinicians to perform a sepsis evaluation and start antibiotic treatment in case of clinical deterioration within the study period.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

Infants born between 24 and 31+6 weeks gestation are eligible for enrollment. Infants at high- or low-risk of early-onset sepsis will be excluded for randomization and included in the observational part of the study. Infants with moderate risk for EOS are randomized 1:1.

Exclusion criteria

Infants at low-risk or high-risk for EOS are not eligible for enrollment in the randomization part of the trial.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-09-2024
Enrollment:	1266
Type:	Actual

Ethics review

Approved WMO Date:	25-06-2024
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
ClinicalTrials.gov	NCT06100614
CCMO	NL85180.018.24