Prospective multicentre observational cohort study on perinatal bacterial infections ;Part 1 of the Netherlands observational study on group B streptococcal disease, bacterial virulence and protective serology (NO GBS)

Published: 12-10-2017
Last updated: 12-04-2024

The primary objectives of the NO GBS study part 1 are to: - determine the clinical characteristics and outcome, and the prevalence of risk factors used by Dutch guidelines for risk assessment in GBS and E. coli meningitis and sepsis cases aged 0-3...

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

Summary

ID

NL-OMON52780

Source
ToetsingOnline

Brief title
Perinatal GBS and E. coli disease in the Netherlands

Condition

- Bacterial infectious disorders
- Central nervous system infections and inflammations
- Neonatal and perinatal conditions

Synonym
baby, GBS, group b stretokokkal, invasive disease, meningitis and sepsis, neonate, S.

agalactiae

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: GBS, Meningitis, Neonate, Sepsis

Outcome measures

Primary outcome

Main study parameter/endpoint

- Clinical characteristics and outcome parameters

- Proportion of cases with risk factors recommended for screening by current and updated Dutch GBS prevention guidelines

- Whole genome sequencing of invasive GBS isolates with Illumina HiSeq at the Wellcome Trust Sanger Institute

Secondary outcome

Secondary study parameters/endpoints

- Comparison of reverse cumulative distributions of specific IgG concentrations determined by enzyme-linked immunosorbent assay (ELISA) against vaccine targets in pregnant women colonized with GBS and mothers of patients with invasive GBS disease

- Comparison of reverse cumulative distributions of specific IgG concentrations determined by ELISA against vaccine targets in newborns from pregnant women colonized with GBS (blood spots and cord blood) and patients with invasive GBS

disease (blood spots and blood)

Study description

Background summary

Streptococcus agalactiae (Group B Streptococcus, GBS) and Escherichia coli are the leading cause of neonatal sepsis and meningitis. One out of five pregnant women is asymptomatically colonized by GBS. Transmission of GBS bacteria to the neonate can result in invasive disease, which has been associated with a case fatality rate of 7%.

Dutch GBS prevention guidelines recommend intrapartum antibiotic prophylaxis for pregnant women with risk factors for GBS disease. We have shown that the incidence of neonatal GBS disease is increasing, despite guideline implementation in 1999. In addition, current guidelines recommend bacterial prophylaxis and treatment for mothers and their children based on a risk-calculation. With this strategy a relatively large group of children is exposed to antibiotics. Another shortcoming of these guidelines is the focus on early onset disease. Late onset disease occurring after 7 days of age is an important problem. The incidence of late onset disease has not changed in the western world over the past decades. Improved risk assessment, a better understanding of GBS pathophysiology and new prevention strategies are needed.

An important future option to reduce invasive disease in neonates is GBS vaccination of mothers during pregnancy. GBS vaccines were shown to be safe and immunogenic in pregnant woman. However, further evaluation of these vaccines is hampered because of the high costs of a phase 3 RCT with clinical endpoints. Therefore, immune correlates of protection are needed to evaluate potential effectiveness of these vaccines.

In this observational cohort study we will determine the sensitivity of Dutch risk-based prevention guidelines to identify cases of invasive disease caused by GBS or E. coli in 0-3 months old patients. Furthermore, we will collect invasive bacterial isolates and blood from patients and their mothers to perform whole genome sequencing of invasive GBS isolates and determine empirical reverse cumulative distributions of specific IgG concentrations against vaccine targets in GBS patients and their mothers. These results will be combined with results from the other parts of the *Netherlands observational study on group b streptococcal disease, bacterial virulence and protective serology (NO GBS)* to discover GBS bacterial virulence genes and determine specific antibody concentrations that protect neonates against invasive GBS disease.

Study objective

The primary objectives of the NO GBS study part 1 are to:
- determine the clinical characteristics and outcome, and the prevalence of risk factors used by Dutch guidelines for risk assessment in GBS and E. coli meningitis and sepsis cases aged 0-3 months in the Netherlands.
- determine the genetic profile of invasive GBS isolates by whole genome sequencing

The secondary objectives are to:
- develop a methodology to measure antibody concentrations against bacterial antigens in dried blood spots;
- determine antibody concentrations against GBS vaccine targets that are correlated with protection against invasive GBS disease.
To accomplish these secondary objectives, the results will be combined with the findings from the other parts of the NO GBS study.

Study design

Prospective observational cohort study

Study burden and risks

The burden on and risk for the baby is limited is negligible. The burden for the mother is minor and the risk minimal

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Newborns

Inclusion criteria

All patients 0-3 months of age with blood or cerebrospinal fluid culture confirmed invasive GBS or E. coli disease in the Netherlands and their mothers are eligible for this study.

Exclusion criteria

Neurosurgical device such as cerebrospinal fluid drain in situ prior to development of meningitis

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-01-2018

Enrollment:	500
Type:	Actual

Ethics review

Approved WMO Date:	12-10-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-08-2018
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-10-2019
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-05-2022
Application type:	Amendment
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	NL63123.018.17