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Feasibility study for the development of a sero-correlate of protection against invasive Group B Streptococcus disease (the iGBS study)

Submission date
02/07/2018

Recruitment status
No longer recruiting

Registration date
09/07/2018

Overall study status
Completed

Last Edited
19/08/2022

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Group B Streptococcus (GBS) is a bacterium (bug) that causes infection in young infants in all regions of the world. Worldwide in 2015 it was estimated that there were at least 319,000 infants under 3 months of age with GBS disease, resulting in 90,000 deaths and at least 10,000 children with long-term disabilities. Babies mostly acquire the GBS bacteria from their mothers around the time of birth and around 20% of all pregnant women carry GBS in their bowel and vagina. The global burden of GBS is therefore high and the options for prevention are currently limited. An effective vaccine that could be given to pregnant women has the greatest potential to benefit mothers and babies worldwide and such vaccines are now being tested in clinical trials, including in pregnant women. To license a new vaccine so that it can be recommended for routine use usually requires evidence that the vaccine is safe and effective in preventing the disease. This usually means undertaking a large trial in which the new vaccine is given to half of the subjects, who are then compared to the other half who did not receive the new vaccine. Such trials are expensive and time-consuming to perform. Another way of licensing a new vaccine is to show that when it is given to relevant groups of people it is able to produce levels of immunity (usually measured as antibodies) in their blood that are known to result in protection. Such levels are called serocorrelates (because they “correlate” with protection). Although there is considerable evidence that high levels of antibody against GBS in pregnant women do correlate with protection against GBS disease in their babies, the precise level (the serocorrelate) is not currently known. Although GBS is the most common cause of serious early infections in UK babies it is still relatively rare overall, so around 150,000 babies will need to be followed in order to find at least 150 babies with GBS disease, which is around the number needed to establish the serocorrelates of protection. The aim of this smaller (feasibility) study of around 4000 women is to assess the recruitment and test the methods. If this feasibility study works well this will lead to a larger study to address the question of how much antibody is needed to protect against invasive infant GBS disease.

Who can participate?
Pregnant women aged 18 and over who are delivering at one of the selected hospitals

What does the study involve?
A small sample of blood is collected from pregnant women and/or from the cord of their newborn babies at delivery and stored in the laboratory. With the cooperation of paediatricians and microbiologists the researchers are alerted if any of the babies develop GBS disease over the next 3 months. For those who do, the level in their blood samples at birth is then compared with that of other babies who did not develop GBS disease. Because many babies acquire GBS from their mothers at birth a smaller number of the mothers have a swab taken to see if they are carrying GBS around the time of birth.

What are the possible benefits and risks of participating?
The antibody tests will help in the development and licensure of GBS vaccines for pregnant women. It is hoped that the results of this study will help to stop babies from becoming sick with GBS disease in the future. A blood sample can cause anxiety for some people and is associated with mild, temporary discomfort. There is a small risk of fainting, bruising and infection. All blood sampling is performed by trained members of the study team. If required, a blood sample may be needed from the baby at 1-3 months (less than a teaspoon full). This can cause discomfort but common distraction techniques, such as breastfeeding, can be used to minimize this. In the unlikely case of a stillbirth, participants are still asked if they are happy to consent for a blood test. This can provide useful information as GBS is a cause of stillbirths.

Where is the study run from?
1. St George’s University Hospitals NHS Foundation Trust (UK)
2. Kingston Hospitals NHS Trust (UK)
3. Croydon University Hospitals NHS Trust (UK)
4. East Surrey Hospitals NHS Trust (UK)
5. Poole Hospital NHS Trust (UK)

When is the study starting and how long is it expected to run for?
June 2018 to August 2020

Who is funding the study?
NIHR Health Technology Assessment Programme (UK)

Who is the main contact?
Prof. Paul Heath

Contact information

Type(s)
Scientific

Contact name
Prof Paul Heath

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Additional identifiers

Protocol serial number
1.0; HTA 17/153/01

Study information

Scientific Title
Feasibility study for the development of a sero-correlate of protection against invasive Group B Streptococcus disease

Acronym
iGBS

Study objectives
What are the Group B Streptococcus (GBS) capsular polysaccharide serotype-specific IgG immunecorrelates of protection against the most prevalent serotypes of GBS causing invasive infant disease (iGBS)?

Aims and objectives:
Given the anticipated study size of this study and its logistic complexities, the aim of this initial feasibility study is to test key operational aspects of the study design of such a study. The feasibility study aims to collect data on maternal GBS colonizing serotype prevalence, anti-capsular IgG concentrations, kinetics of antibody transfer and IgG decay in the first three months of life and enable sample size and power assumptions for the main study to be assessed.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands - Solihull, 15/06/2018, REC ref: 18/WM/0147

Study design
Multicentre prospective cohort study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Invasive infant disease caused by Group B Streptococcus

Interventions

The trialists will establish maternal delivery/infant cord serum collection from 5 maternity units (around 4000 women) and test the feasibility of their strategies. They will collect a small sample of blood from pregnant women and/or from the cord of their newborn babies at delivery and store these samples in the laboratory. With the cooperation of paediatricians and microbiologists they will be alerted if any of the babies develop GBS disease over the next 3 months (cases). For those who do, the trialists can then compare the level in their blood samples at birth with that of other babies (controls) who did not develop GBS disease.

Because many babies acquire the GBS from their mothers at birth the trialist will also carry out a sub-study in which 1000 mothers will have a vaginal-rectal swab taken to see if they are carrying GBS around the time of birth. The babies of mothers identified as carrying GBS will be the control babies as they were known to be exposed to GBS at birth but didn't develop GBS disease.

The trialists will assess the following parameters:
1. Enrollment rate (the rate (proportion) of eligible women who are willing to participate in the blood collection study)
2. Maternal and/or cord blood collection rate
3. The impact of different timings related to blood sample processing and storage
4. Key clinical data collection rate
5. Rectovaginal swab/delivery blood sample study enrollment rate
6. Rectovaginal swab and delivery blood sample collection rate
7. Infant blood sample study consent rate
8. Infant surveillance consent rate
The collection of blood samples in colonised women will be used to derive estimates of GBS anticapsular IgG concentrations using a standardised assay.

Intervention Type
Other

Primary outcome(s)
The feasibility of collecting serum at delivery (either maternal or cord or both) from a large cohort of pregnant women, assessed using:
1. Enrolment rate (the rate (proportion) of eligible women who are willing to participate in the delivery blood collection study)
2. Maternal and/or cord blood collection rate
3. Key clinical exclusion data (gestation at birth, receipt of IAP in labour (yes/no), type of IAP (list), time between administration of IAP and delivery (in hours) collection rate)
4. Infant iGBS surveillance consent rate

Key secondary outcome(s))
In the sub-study the following are assessed at delivery:
1. Rectovaginal swab study consent rate
2. Rectovaginal swab collection rate
3. Rectovaginal GBS colonisation rate
4. Rectovaginal GBS CPS serotype-specific colonisation rates

In the sub-study where samples of maternal/cord blood and rectovaginal swabs are available, the following are assessed at delivery:
1. Infant blood sample study consent rate
2. Infant Guthrie card consent rate
3. Infant Guthrie card collection rate

Completion date
31/08/2020

Eligibility

Key inclusion criteria
1. Pregnant
2. ≥ 18 years of age
3. Delivering at one of the selected hospitals
4. Consented to participate during the study period

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Total final enrolment
1823

Key exclusion criteria
Does not meet the inclusion criteria

Date of first enrolment
02/07/2018

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St George’s University Hospitals NHS Foundation Trust
Blackshaw Road

London
United Kingdom
SW17 0QT

Study participating centre
Kingston Hospitals NHS Trust
Galsworthy Rd
Kingston upon Thames
Kingston
United Kingdom
KT2 7QB

Study participating centre
Croydon University Hospitals NHS Trust
530 London Rd
Croydon
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CR7 7YE

Study participating centre
East Surrey Hospitals NHS Trust
Canada Ave
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United Kingdom
RH1 5RH

Study participating centre
Poole Hospital NHS Trust
Longfleet Rd
Poole
United Kingdom
BH15 2JB

Sponsor information

Organisation
St George's University Hospitals NHS Foundation Trust

ROR

https://ror.org/039zedc16

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
All data will be stored in an online format on the RedCap database. Data in this database will be anonymised, with each participant being identified by a unique participant ID. No patient identifiable information will be stored on RedCap. Research midwives and members of the research team all have secure password protected accounts that allow them to input data onto this form.

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2019	20/12/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 9.0	06/10/2020	19/08/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes