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Accuracy of a rapid intrapartum test for maternal group B streptococcal colonisation and its potential to reduce antibiotic usage in mothers with risk factors

Submission date
15/04/2015

Recruitment status
No longer recruiting

Registration date
16/04/2015

Overall study status
Completed

Last Edited
24/02/2022

Condition category
Pregnancy and Childbirth

[X] 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 the leading cause of serious infection in newborn babies in developed countries. It is transmitted to babies around birth from mothers who carry the bacterium (bug) in their bowels and vagina without any symptoms. Antibiotics given to the mother from the start of labour reduces the risk of the newborn baby developing early onset GBS disease, both by reduction of the chance of transmission and by giving the baby protective antibiotics before birth, providing they are given for long enough before delivery. Medical bodies recommend that preventative antibiotics should only be given in labour to mothers with risk factors for transmitting the infection to their baby. The babies of these mothers may then be investigated and some may be treated with antibiotics for GBS infection, particularly where more than one risk factor is present. The vast majority of these babies do not have GBS infection and are unnecessarily exposed to antibiotics, separated from their mothers for investigations and kept in hospital. Unnecessary use of antibiotics can also promote the evolution of antibiotic resistant strains of bacteria, so called “superbugs”. The aim of this study is to establish whether rapid testing technology which determines whether the mother is carrying GBS can be used to direct the appropriate and timely administration of preventative antibiotics.

Who can participate?
We will identify around 1,340 mothers in labour who have risk factors for GBS infection in their newborn babies in at least 16 hospitals in the West Midlands and London during a 4-6 week study period.

What does the study involve?
In half of the hospitals, all higher-risk women will be cared for as per current guidance, which would be with antibiotics. In the other hospitals, all women with GBS risk factors will have a swab taken from their vagina and rectum, to be used in the rapid test. In these hospitals, antibiotics will only be given in labour if the rapid test result is positive. If the rapid test result fails to deliver a result within 55 minutes, or the woman's care team suspect an infection then

women will be given antibiotics as per national GBS guidelines. In another aspect of the study we will assess the accuracy of the rapid testing, namely does it always give a positive result for women carrying GBS and negative results for those who are not. We will also determine whether the test is practical to use on a busy labour ward and give results in time for antibiotics to be given to those who need them. We will compare whether using giving antibiotics in labour based on the rapid test result, rather than giving antibiotics to all those with risk factors, results in a reduction in antibiotic usage. The impact of the two antibiotic strategies will be evaluated by measuring how many babies are found to be carrying GBS at birth and the rates of GBS infection in the first six days of the babies' lives. We will determine which strategy offers the best value for money by calculating the costs and benefits of each. Finally, we will grow any GBS bacteria collected from mothers and their babies in laboratory and test whether any antibiotic resistant strains are found.

What are the possible benefits and risks of participating?
This study is looking to see if a small enhancement to the normal treatment pathway allows better direction of antibiotic administration to women in labour. As the normal treatment pathway is still largely followed, and the clinicians can prescribe antibiotics at any time they wish, there are no real risks in taking part. The benefit of taking part in the test group is that you are unlikely to be prescribed antibiotics if you are not colonised with GBS.

Where is the study run from?
At least 16 hospitals in the West Midlands and London (UK).

When is the study starting and how long is it expected to run for?
May 2016 to October 2019

Who is funding the study?
National Institute for Health Research (UK).

Who is the main contact?
Emily Dixon (Trial Manager)
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Study website
https://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/portfolio-v/GBS2/

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Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 13/82/04

Study information

Scientific Title
Accuracy of a rapid intrapartum test for maternal group B streptococcal colonisation and its potential to reduce antibiotic usage in mothers with risk factors

Acronym
GBS2

Study objectives
Current study hypothesis as of 26/04/2018:
1. To establish the real time accuracy of the GeneXpert rapid test for GBS colonisation among women presenting to a labour ward with risk factors associated with GBS transmission, comparing against the reference standard of selective enrichment culture, in a prospective

cohort study.
2. To evaluate if rapid GBS testing reduces maternal and neonatal antibiotic usage, compared with usual care administration of Intrapartum Antibiotic Prophylaxis (IAP) is directed based on maternal risk factors alone, in a cluster randomised trial.

Previous study hypothesis:
To see if a rapid test for GBS used in pregnant women with risk factors for colonisation with GBS2 undergoing a trial of labour will reduce the use of intrapartum antibiotics.

More details and protocol can be found at: https://www.journalslibrary.nihr.ac.uk/programmes/hta/138204/#/

Ethics approval required
Old ethics approval format

Ethics approval(s)
The West Midlands – Edgbaston Research Ethics Committee, 09/03/2016, ref: 16/WM/0036

Study design
A prospective test accuracy cohort study, a cluster randomised controlled trial, and a health economic evaluation

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet

Health condition(s) or problem(s) studied
Early onset group B streptococcus infection in the neonate

Interventions
We will identify around 1,340 mothers in labour who have risk factors for GBS infection in their newborn babies in at least 16 hospitals in the West Midlands and London during a 4-6 week study period. In half of the hospitals, all higher-risk women will be cared for as per current guidance, which would be with antibiotics. In the other hospitals, all women with GBS risk factors will have a swab taken from their vagina and rectum, to be used in the rapid test. In these hospitals, antibiotics will only be given in labour if the rapid test result is positive. If the rapid test result fails to deliver a result within 55 minutes, or the woman's care team suspect an infection then women will be given antibiotics as per national GBS guidelines.

In another aspect of the study we will assess the accuracy of the rapid testing, namely does it always give a positive result for women carrying GBS and negative results for those who are not.

We will also determine whether the test is practical to use on a busy labour ward and give results in time for antibiotics to be given to those who need them. We will compare whether using giving antibiotics in labour based on the rapid test result, rather than giving antibiotics to all those with risk factors, results in a reduction in antibiotic usage. The impact of the two antibiotic strategies will be evaluated by measuring how many babies are found to be carrying GBS at birth and the rates of GBS infection in the first six days of the babies' lives. We will determine which strategy offers the best value for money by calculating the costs and benefits of each. Finally, we will grow any GBS bacteria collected from mothers and their babies in laboratory and test whether any antibiotic resistant strains are found.

Intervention Type
Other

Primary outcome measure
Current primary outcome measure as of 26/04/2018:
The primary outcome measure for the randomised controlled trial part of the study is the proportion of women receiving IAP for GBS prophylaxis, of all those identified with one or more risk factors for GBS transmission. This is defined as those women receiving IAP which has been indicated for GBS prophylaxis (regardless of whether there is another reason for antibiotic administration), as a proportion of those identified by the delivery suite midwives as having one or more risk factors for GBS transmission.

Previous primary outcome measure:
To evaluate if rapid intrapartum GBS testing reduces maternal and neonatal antibiotic usage, compared with usual care where Intrapartum Antibiotic Prophylaxis (IAP) is directed based on maternal risk factors alone.

Secondary outcome measures
Current secondary outcome measures for the randomised controlled trial part of the study as of 01/05/2018:
1. Intrapartum maternal antibiotic use for any indication, defined as those women receiving IAP for GBS prophylaxis, for a maternal clinical indication such as pyrexia, on maternal request, prior to caesarean section or any other reason as identified by delivery suite midwives as having one or more risk factors for GBS transmission.
2. Intrapartum maternal antibiotic use for any indication other than caesarean section, defined as women receiving intrapartum antibiotic for GBS prophylaxis, for a maternal clinical indication such as pyrexia, on maternal request, or for any other reason other than for caesarean section as identified by delivery suite midwives as having one or more risk factors for GBS transmission.
3. Neonatal antibiotic use for prophylaxis or treatment, defined as babies receiving antibiotic prophylaxis due to maternal GBS status or antibiotic treatment for suspected or confirmed neonatal infection as identified by delivery suite midwives as having one or more risk factors for GBS transmission.
4. Post-partum maternal antibiotics use for any indication, defined as those women receiving post-partum antibiotic which has been indicated as being a maternal clinical indication such as pyrexia, on maternal request, or for any other reason, as identified by the delivery suite midwives as having one or more risk factors for GBS transmission. The period where this data will be collected is from delivery until the mother's discharge from either delivery hospital or from any hospital where they were immediately transferred. Antibiotic use data following any re-admittance or prescribed from a general practitioner will not be used.
5. Time of IAP exposure, defined as the duration between the start time of the first dose of IAP and the delivery of the baby. Sufficient exposure will be considered as an interval of either >2 h

or >4 h before delivery.
6. Time taken to act on rapid test results. Exploratory assessment of the practical challenges of implementing a rapid test policy. To determine the duration between a positive test becoming available on the GeneXpert machine and the time the result is collected by a midwife, and the duration between that point and the start of IAP. Reasons for variation between sites will be explored.
7. Neonatal GBS colonisation rates. The rate of GBS positive enriched cultures from the neonatal ear swabs as a proportion of all neonatal ear swabs cultured.
8. Neonatal infection. Neonatal infection rates will be derived from the number of babies prescribed antibiotics for presumed neonatal infection, as a proportion of all live born babies.
9. Neonatal mortality. Mortality rates will include stillbirth rate, early neonatal death (before 7 days) rate and these combined as the perinatal mortality rate, for both confirmed early onset GBS disease and for all causes.
10. Serious adverse events

Previous secondary outcome measures for the randomised controlled trial part of the study as of 26/04/2018:
1. Intrapartum maternal antibiotic use for any indication, defined as those women receiving IAP for GBS prophylaxis, for a maternal clinical indication such as pyrexia, on maternal request, prior to caesarean section or any other reason as identified by delivery suite midwives as having one or more risk factors for GBS transmission.
2. Intrapartum maternal antibiotic use for any indication other than caesarean section, defined as women receiving intrapartum antibiotic for GBS prophylaxis, for a maternal clinical indication such as pyrexia, on maternal request, or for any other reason other than for caesarean section as identified by delivery suite midwives as having one or more risk factors for GBS transmission.
3. Neonatal antibiotic use for prophylaxis or treatment, defined as babies receiving antibiotic prophylaxis due to maternal GBS status or antibiotic treatment for suspected or confirmed neonatal infection as identified by delivery suite midwives as having one or more risk factors for GBS transmission.
4. Post-partum maternal antibiotics use for any indication, defined as those women receiving post-partum antibiotic which has been indicated as being a maternal clinical indication such as pyrexia, on maternal request, or for any other reason, as identified by the delivery suite midwives as having one or more risk factors for GBS transmission. The period where this data will be collected is from delivery until the mother’s discharge from either delivery hospital or from any hospital where they were immediately transferred. Antibiotic use data following any re-admittance or prescribed from a general practitioner will not be used.
5. Time of IAP exposure, defined as the duration between the start time of the first dose of IAP and the delivery of the baby. Sufficient exposure will be considered as an interval of either >2 h or >4 h before delivery.
6. Time taken to act on rapid test results. Exploratory assessment of the practical challenges of implementing a rapid test policy. To determine the duration between a positive test becoming available on the GeneXpert machine and the time the result is collected by a midwife, and the duration between that point and the start of IAP. Reasons for variation between sites will be explored.
7. Neonatal GBS colonisation rates. The rate of GBS positive enriched cultures from the neonatal ear swabs as a proportion of all neonatal ear swabs cultured.
8. Neonatal infection. Neonatal infection rates will be derived from the number of babies prescribed antibiotics for presumed neonatal infection, as a proportion of all live born babies.
9. Neonatal mortality. Mortality rates will include stillbirth rate, early neonatal death (before 7 days) rate and these combined as the perinatal mortality rate, for both confirmed early onset GBS disease and for all causes.

Current secondary outcome measures for the test accuracy part of the study as of 26/04/2018:
1. Measures of test accuracy. The sensitivity, specificity, positive and negative predictive values of the GeneXpert GBS rapid test, using the enriched culture as the reference standard.
2. Failure of test. The proportion of the cartridges on which the tests were not commenced within 15 minutes of inoculation. The proportion of tests initiated on the Cepheid GeneXpert machine which failed to produce a result within 55 minutes, or flagged as 'failed' by the system will indicate the utility of the test as a rapid, point of care test on a labour ward.

Previous secondary outcome measures:
1. To establish the real time accuracy of the rapid test for GBS colonisation among women in labour with risk factors for GBS transmission, comparing against the reference standard of selective enrichment culture
2. To establish a standard operating procedure for use of a rapid, point-of-care intrapartum test for GBS colonisation (GeneXpert) on a labour ward with turnaround times compatible with provision of a suitable duration of antibiotic exposure to test positive mothers
2. To determine the time to availability of test results in practice and the time remaining before birth are suffcient to give an adequate antibiotic exposure for effective prevention of GBS transmission from colonised mothers to their newborn child
3. To explore the impact of testing strategies on neonatal outcomes
4. To determine the effect of peripartum antibiotic exposure on the risk of carriage of antibiotic resistant bacteria in infants at up to 6 weeks of age
5. To determine the cost and cost-effectiveness of rapid intrapartum GBS testing for preventing early-onset neonatal GBS disease in women with risk factors for GBS transmission against usual care of risk factor directed IAP

Overall study start date
01/05/2016

Completion date
31/10/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 26/04/2018:
Presence of one or more of the following risk factors will define inclusion of the mother and baby into the study:
1. Previous baby with early or late onset neonatal GBS disease as reported by the mother and documented in the maternal notes.
2. GBS bacteriuria during current pregnancy, as documented in the maternal notes, irrelevant of whether the GBS bacteriuria was treated at the time of diagnosis with antibiotics.
3. GBS colonisation of the vagina and/or rectum (determined from a vaginal/rectal swab) in current pregnancy, as documented in the maternal notes.
4. Preterm labour (<37 weeks' gestation), with intact membranes or rupture of membranes of any duration, whether suspected, diagnosed or established.
5. Maternal pyrexia (>38°C) observed at any point in labour, including clinically suspected /confirmed chorioamnionitis

Previous inclusion criteria:
Presence of one or more of the following risk factors will define inclusion of the mother and baby into the study:

1. The mother has delivered a previous baby who developed neonatal GBS disease (early or later onset), as reported by the mother and documented in the maternal notes
2. GBS bacteriuria during the current pregnancy, as documented in the maternal notes, irrelevant of whether the GBS bacteriuria was treated at the time of diagnosis with antibiotics
3. GBS colonisation of the vagina and/or the rectum (determined from a recto/vaginal swab) in current pregnancy, as documented in the maternal notes
4. Maternal pyrexia (>38°C) observed at any point in labour, or clinically suspected/confirmed chorioamnionitis
5. Preterm labour with prelabour rupture of membranes of any duration
6. Preterm labour if there is suspected or confirmed intrapartum rupture of membranes lasting more than 18 hours

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Minimum 1720 (86 per cluster, 10 clusters per arm, 2 arms to the trial)

Total final enrolment
1625

Key exclusion criteria
Current participant exclusion criteria as of 01/05/2018:
Those who do not have any of the risk factors associated with an increased risk of being colonised by GBS

Previous participant exclusion criteria as of 26/04/2018:
1. Aged under 16 years
2. Women in labour at a gestation age of <24 weeks
3. Women who, on arrival at the maternity unit, are already in second stage labour or who are likely to deliver their baby imminently
4. Women whose baby is known to have died in utero or who has a congenital anomaly incompatible with survival at birth
5. Women having an elective Caesarean delivery, which will be performed even if presenting in labour

Previous participant exclusion criteria:
Those who do not present with any of the risk factors associated with an increased risk of being colonised by GBS

Date of first enrolment
01/08/2017

Date of final enrolment
30/04/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Royal London Hospital
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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B18 7QH

Study participating centre
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CV2 2DX

Study participating centre
Nottingham University Hospitals NHS Trust
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Study participating centre
Heart of England NHS Foundation Trust
Bordesley Green East
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B9 5SS

Study participating centre
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Study participating centre
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Walsall Manor Hospital

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Study participating centre
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E9 6SR

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Maidstone and Tunbridge Wells NHS Trust
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Study participating centre
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Study participating centre
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Study participating centre

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Sponsor information

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Sponsor type
University/education

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
31/10/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file		08/06/2017	20/07/2017	No	No
Protocol file	version v3	20/12/2017	26/04/2018	No	No
Protocol file	version V4.0	18/10/2018	21/05/2019	No	No
Results article		14/01/2022	18/01/2022	Yes	No
Funder report results		01/02/2022	24/02/2022	Yes	No
HRA research summary			28/06/2023	No	No