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Pharmacogenetics to avoid loss of hearing

Submission date 18/04/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 25/04/2019	**Overall study status** Completed	
Last Edited 06/05/2025	**Condition category** Neonatal Diseases	

Plain English summary of protocol

Background and study aims
Gentamicin is an antibiotic that is routinely used to treat or protect against infection in over 95% of babies admitted to Neonatal Intensive Care Units (NICUs). Some children have a genetic change (variant) that predisposes to severe hearing loss or total deafness after a single dose of gentamicin. About 1 in 500 people have this variant. Groups with a higher risk of repeated chest infections throughout their lives (i.e. people with cystic fibrosis) are routinely tested for this variant using a technique known as pyrosequencing. This current test takes at least three days to return a clinically relevant result. Newborn babies with suspected sepsis should be treated within the first hour of suspicion. The current genetic test is therefore unsuitable in this situation. The researchers have developed a point-of-care test (PoCT) to detect this genetic variant via a buccal (mouth) swab, delivering a reliable result in less than 40 minutes. This study aims to trial this new genetic testing approach in two large newborn intensive care units (NICUs). The aim is to assess the performance of this device in providing an accurate result, in a time that will indicate if the child can or cannot be treated with gentamicin (a safe alternative can be used), and therefore avoid the risk of deafness.

Who can participate?
Babies admitted to the NICU or requiring a screen for infection within 72 hours of birth

What does the study involve?
All participating babies are tested for the genetic variant before antibiotic treatment. There is no follow up as part of the study.

What are the possible benefits and risks of participating?
Babies included in this study will benefit from a rapid, non-invasive genetic test which will allow personalised antibiotic prescribing to avoid hearing loss in at-risk individuals. If successful, the use of this technology across the UK could avoid permanent, severe hearing loss in about 180 babies every year.

Where is the study run from?
1. Manchester University NHS Foundation Trust (UK)
2. Liverpool Women's NHS Foundation Trust (UK)

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

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

Who is the main contact?
Dr Rachel Mahood
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Contact information

Type(s)
Public

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)

253102

Protocol serial number
B00321, IRAS 253102

Study information

Scientific Title
Pharmacogenetics to avoid loss of hearing (clinical implementation study)

Acronym
PALOH

Study objectives
A clinical implementation study to critically assess the use of a novel point-of-care pharmacogenetic testing device to detect neonates at risk of aminoglycoside-induced hearing loss secondary to the genetic variant m.1555A>G. The primary objective is to assess the performance of the device and any barriers to implementation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Current ethics approval as of 04/11/2019:
Approved 22/08/2019, North West - Liverpool East Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ; nrescommittee.northwest-liverpooleast@nhs.net), ref: 19/NW/0400

Previous ethics approval:
NHS Health Research Authority Research Ethics Service - approval pending

Study design
Multi-centre clinical feasibility study

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied
Neonatal intensive care

Interventions
This study involves the use of a novel genetic test to detect the m.1555A>G variant which is associated with aminoglycoside-induced hearing loss. All neonates admitted to the participating neonatal intensive care units during the study period will be tested for this variant prior to antibiotic treatment, to allow personalised prescribing and avoiding permanent, irreversible hearing loss in at-risk individuals.

The intervention is a one-off genetic test at the point of admission to neonatal intensive care. The objective is to look at feasibility of incorporating the test into the current clinical pathway rather than the efficacy of the intervention, which is already known. There is no follow up period as part of the study.

Intervention Type
Genetic

Primary outcome(s)
The total number of neonates who are successfully tested for the m. 1555A>G genetic variant out of all babies given antibiotics on admission or assessment in the two participating sites, measured using patient medical notes and real-time data collection at the end of the study period

Key secondary outcome(s))
1. The total number of neonates identified with the m. 1555A>G genetic variant, measured using retrospective data collection from device at the end of the study period
2. Average time from admission to antibiotic administration for all participants tested throughout the 6-month study period, measured using patient medical notes and real-time data collection
3. Total number of incidences where time to antibiotic administration exceeds the 60-minute target and the reasons for these, measured using patient medical notes and real-time data collection
4. Total number of assay failures within the 6-month testing period and the reasons for these, measured using retrospective data collection from device
5. Resource impact: additional staff time required to secure samples and undertake testing, measured using staff observations
6. Total number of babies where testing was not undertaken during the 6-month testing period and the reasons for these, measured using patient medical notes and real-time data collection
7. The overall correlation of the point-of-care testing result with the current in-house reference assay (pyrosequencing)

Completion date
30/11/2020

Eligibility

Key inclusion criteria
1. All babies admitted to NICU at Manchester University NHS Foundation Trust (MFT, Oxford Road Campus) and Liverpool Women's NHS Foundation Trust (LWH), for 6 months commencing from the trial start date
2. Babies requiring a screen for infection within 72 hours of birth (an infection screen for suspected early onset neonatal infection) at LWH who are not formally admitted to the neonatal unit, for 6 months commencing from the trial start date

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Total final enrolment
751

Key exclusion criteria
Neonates requiring antibiotics immediately with already established IV access

Date of first enrolment
01/01/2020

Date of final enrolment
30/11/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Manchester University NHS Foundation Trust
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Liverpool Women's NHS Foundation Trust
Liverpool Women’s Hospital
Crown Street
Liverpool
United Kingdom
L8 7SS

Sponsor information

Organisation

Manchester University NHS Foundation Trust

ROR
https://ror.org/00he80998

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

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. William Newman (William.newman@manchester.ac.uk). Data pertaining to clinical timings associated with testing (e.g. time of NICU admission, time of swab, time of antibiotic administration etc) can be provided to researchers upon request to CI Prof Newman. Data will be anonymised. Consent for this data collection was presumed under an “opt-out” consent model.
The datasets generated and/or analysed during the current study will be included in the subsequent results publication.

IPD sharing plan summary
Available on request, Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Qualitative study	07/01/2024	08/01/2024	Yes	No

Results article	21/03/2022	06/05/2025	Yes	No
Protocol article	16/06/2021	18/06/2021	Yes	No
HRA research summary		28/06/2023	No	No
Other publications	23/07/2020	06/05/2025	Yes	No
Other publications	22/01/2021	06/05/2025	Yes	No