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Study of antimicrobial resistance in patients receiving outpatient parenteral antimicrobial therapy

Submission date
18/02/2020

Recruitment status
No longer recruiting

Registration date
20/02/2020

Overall study status
Completed

Last Edited
20/06/2024

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
Bacteria that are resistant to antibiotics are becoming an important problem in hospitals and much research has been carried out to try to reduce the rates. Unwell patients in hospital who have received long antibiotic courses have a high risk of developing infections with antibiotic-resistant bacteria. Patients who are in the community and have received long courses of antibiotics may be at risk but few studies have been done to explore this. Therefore, this study will help clinicians understand how gut bacteria changes, and may become more resistant, after a long course of antibiotics, in a community-based population. In the future this could help clinicians choose better antibiotics for each individual patient. It could help stop the spread of antibiotic-resistant bacteria in hospital by showing when clinicians need to use special infection control measures such as the use of gloves, aprons or gowns, or ensuring certain patients have their own toilet or room.

Who can participate?
Patients aged 18 or older who are expected to receive 2 or more weeks of IV antibiotics, and Infectious Diseases ward or clinic patients who have received no antimicrobial therapy within the last 3 months

What does the study involve?
This study explores how gut bacteria change and develop resistance in patients who have received long courses of intravenous antibiotics in the community. It compares bacteria in stool from participants who have received different intravenous antimicrobials (Outpatient Parenteral Antimicrobial Therapy (OPAT) patients) to participants who have not (a control group). Stool samples will be examined at enrolment, weekly during antimicrobial therapy, at 3 and 6 months. The OPAT group will provide a minimum of 4 stool samples and the control group will provide 3 stool samples. The OPAT group will provide more stool samples than the control group as they will have additional weekly stool samples collected at the time of their routine OPAT clinic visits. All stool samples will be self-collected by the participant and then handed to the study team. At the start of the study, the study team will collect the participant's clinical information from the medical records. This will include the following information: NHS number, date of birth, gender,

ethnicity, weight, smoking status, alcohol intake, dietary requirements, probiotic or prebiotic use, travel abroad, contact with hospital in the last year, medical/surgical history, antibiotic use, medication history and any relevant symptoms they may have (such as diarrhoea or vomiting.) The weekly face-to-face return visits to OPAT clinic are part of the usual care if the participant is receiving therapy. At return visits the participant will be asked about any relevant symptoms they may have (such as diarrhoea or vomiting,) any new hospital contact, infections or recent antibiotics they may have received since their last visit. The 3 and 6 month follow up visits may be completed face-to-face or remotely, via telephone consultation, with the study team member. At 3 and 6 month return visits the participant will be asked about any relevant symptoms they may have (such as diarrhoea or vomiting), any new hospital contact, infections or recent antibiotics they may have received since their last visit. The 6-month visit marks the end of the study period for each participant.

What are the possible benefits and risks of participating?
There are no direct benefits to participants for taking part in the study. However, the information that the study team obtain from the study may help future patients and enable doctors to reduce the spread of antibiotic-resistant gut bacteria. There are no direct risks to participants if they take part in this study. There may be some inconvenience associated with the donation of stool samples during the study, as they need to be dropped off at the clinic, at the 3 and 6 month follow up period, by the participant, friend or family member. If the participant is found to have antibiotic-resistant gut bacteria they will be informed and should not be concerned. This information will be recorded in their medical electronic records so that it can be used in the future to ensure they receive the right antibiotics and, if necessary, access to a private room.

Where is the study run from?
Addenbrooke's Hospital, CUH NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
September 2019 to August 2021

Who is funding the study?
1. Academy of Medical Sciences and the Health Foundation (UK)
2. National Institute for Health Research (UK)

Who is the main contact?
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Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
273856

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
A095421, IRAS 273856

Study information

Scientific Title
Evolution of antimicrobial resistance in patients receiving outpatient parenteral antimicrobial therapy

Acronym
Study of AMR in OPAT patients

Study objectives

1. How does the gut bacteria change, and does it become more resistant, after a long course of antibiotics in a community-based group of patients compared to those that have not received any antibiotics?
2. Specifically, are there differences that can be detected by testing for gut bacteria's antibiotic-resistance genes and does this difference affect the patient's health by increasing the chance of difficult-to-treat infections?
3. Also, are there differences we can detect by looking for the presence of resistant bacteria including multi-drug resistant organisms (MDRO) and does this difference affect the patient's health by increasing the chance of difficult to treat infections?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/01/2020, East Midlands - Derby Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; Tel: +44 (0)2071048285; Email: NRESCommittee.EastMidlands-Derby@nhs.net), REC ref: 20/EM/0009

Study design
Prospective observational cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Antimicrobial resistance (AMR)

Interventions
This study involves 4 groups. Each group contains 10 patients:
Group 1: have not received intravenous antimicrobials
Group 2: have received the intravenous antimicrobial ceftriaxone
Group 3: have received the intravenous antimicrobial ertapenem
Group 4: have received the intravenous antimicrobial daptomycin

Eligible participants will have been approached by a study team member during routine clinical care, will have discussed the study, and been provided with written information: the Participant Information leaflet. Participants who decide to take part in the study will sign a Consent form at enrolment.

The study team will collect stool samples from participants at the start of the study and later at approximately 3 and 6 months. The Outpatient Parenteral Antimicrobial Therapy (OPAT) group will provide a minimum of 4 stool samples and the "control" group will provide 3 stool samples. The OPAT group will provide more stool samples than the control group as they will have additional weekly stool samples collected at the time of their routine OPAT clinic visits. All stool samples will be self-collected by the participant and then handed to the study team.

At the start of the study, the study team will collect the participant's clinical information from the medical records. This will include the following information: NHS number, date of birth,

gender, ethnicity, weight, smoking status, alcohol intake, dietary requirements, probiotic or prebiotic use, travel abroad, contact with hospital in the last year, medical/surgical history, antibiotic use, medication history and any relevant symptoms they may have (such as diarrhoea or vomiting).

The weekly face-to-face return visits to OPAT clinic are part of the usual care if the participant is receiving therapy. At return visits the participant will be asked about any relevant symptoms they may have (such as diarrhoea or vomiting), any new hospital contact, infections or recent antibiotics they may have received since their last visit.

The 3 and 6 month follow up visits may be completed face-to-face or remotely, via telephone consultation, with the study team member. At 3 and 6 month return visits the participant will be asked about any relevant symptoms they may have (such as diarrhoea or vomiting,) any new hospital contact, infections or recent antibiotics they may have received since their last visit. The 6-month visit marks the end of the study period for each participant.

Intervention Type
Other

Primary outcome(s)
1. Number of participants with stool carriage of specific Antimicrobial Resistance Genes (ARGs), measured using DNA/RNA extraction and testing using multiplex PCR for selected targets, at baseline, during antimicrobial therapy, and at 3 and 6 months
2. Number of participants with phenotypic evidence of Antimicrobial Resistance (AMR) organisms, measured using chromogenic agar for CPE, ESBL and VRE with resistant organisms undergoing identification using MALDI TOF MS (Bruker) and antimicrobial susceptibility testing using the Vitek-2 system (BioMerieux), at baseline, during antimicrobial therapy, and at 3 and 6 months
3. Number of participants with significant changes in the faecal microbiome diversity, measured using DNA library preparation and high-throughput microbial whole-genome sequencing, at selected timepoints including, for example, at baseline and 3 and 6 months

Key secondary outcome(s))
1. Risk factors for carriage of ARGs, measured using correlation between the presence of ARGs and the presence of certain clinical characteristics at baseline
2. Clinical outcomes of patients with AMR organisms (e.g. clinical deterioration or death), measured using correlation between the presence of AMR organisms and the presence of certain clinical characteristics, within the 6-month follow-up period

Completion date
18/08/2021

Eligibility

Key inclusion criteria
1. Adult (age 18 years older)
2. Male or female
3. Cases: patients expected to receive 2 or more weeks of IV antibiotics
4. Controls: an Infectious Diseases ward or clinic patient who has received no antimicrobial therapy within the last 3 months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
40

Key exclusion criteria
1. Patients with known previous MDRO colonisation (e.g. ESBL, CPE, VRE)
2. Those known to be pregnant
3. Does not fulfil study inclusion criteria
4. Declines or are unable to consent

Date of first enrolment
19/02/2020

Date of final enrolment
21/04/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Addenbrooke's Hospital, CUH NHS Foundation Trust
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Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Funder(s)

Funder type
Government

Funder Name
Academy of Medical Sciences and the Health Foundation

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 dataset will be held at Addenbrooke's Hospital, CUH NHS Foundation Trust, UK. It will not be made fully available as the dataset will contain patient identifiable information and clinical details regarding medical conditions and treatment outcomes.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other unpublished results			20/06/2024	No	No
Participant information sheet	Participant information sheet version 2.0	11/11/2025	11/11/2025	No	Yes
Protocol file		23/01/2020	16/09/2022	No	No