ISRCTN11133689 https://doi.org/10.1186/ISRCTN11133689

Do food supplements containing live bacteria (probiotics) reduce or stop a particular infection (CPE) living in the bowel?

Submission date
07/08/2019

Recruitment status
No longer recruiting

Registration date
30/08/2019

Overall study status
Completed

Last Edited
30/08/2019

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Antibiotic resistance of Gram-negative bacteria, particularly the Enterobacteriaceae, is a major global concern. Manchester is known to have a higher spread of carbapenem-resistant Klebsiella pneumoniae which combines virulence, high transmissibility and transmissible resistance to almost all antibiotics. Traditional approaches, such as antimicrobial stewardship and infection control, are unlikely to reverse the spread of carbapenem-resistant Enterobacteriaceae. The probiotic species Lactobacillus reuteri inhibits Enterobacteriaceae and its administration reduces their counts in the infant gut. It is now used in paediatric practice to treat carriage of resistant strains of Enterobacteriaceae, including Klebsiella pneumoniae. This is a study in Manchester of immuno-competent adults known to be colonised with multi-resistant K pneumoniae. The aim is to investigate whether any falls in faecal counts of multi-resistant K pneumoniae seen after the administration of a probiotic are greater than any falls seen in the control group. The study will also investigate whether a lower proportion of the final faecal samples from probiotic-receiving than from control participants yield multi-resistant K pneumoniae on culture.

Who can participate?
Patients aged 18 or older who are immuno-competent and colonised with multi-resistant K pneumoniae

What does the study involve?
Participants are randomly allocated to be discharged from hospital with a prescription of 1 chewable probiotic tablet to take each day for 21 days, or no additional tablets at all. All participants, regardless of having been asked to take the probiotic tablet or not, need to return a faecal sample to the hospital 21 days after they have returned home from their stay. Participants are given a kit to post this sample and instructions on how to do this. The kits are pre-paid for so it does not cost participants anything to post the sample. A Research Nurse from the hospital calls participants to remind them to send the sample and also ask questions about how the participant is feeling and to check that they have taken all probiotic tablets (if allocated to this group)

What are the possible benefits and risks of participating?
There will be no direct benefit to taking part in this study. However, it is hoped that the information from this study will show the impact probiotics have on the gut count of multiresistance bacteria in the gut for future investigations. It is not expected that the participants will experience any serious adverse events related to the probiotic. These products are considered to be food and are safe for consuming. There are a number of studies with children and adults supporting this. No other risks are identified.

Where is the study run from?
1. Manchester Royal Infirmary (UK)
2. Wythenshawe Hospital (UK)

When is the study starting and how long is it expected to run for?
November 2018 to December 2019

Who is funding the study?
Healthcare Infection Society (UK)

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
B00261

Study information

Scientific Title
Randomised open-label controlled feasibility trial of probiotic in the elimination of faecal carriage carbapenemase-bearing Klebsiella pneumoniae

Acronym
PITFALL

Study objectives
1. To investigate whether any falls in faecal counts of a carbapenemase-bearing Klebsiella pneumoniae seen after 21 days of probiotic (Lactobacillus reuteri) administration to adults are greater than any falls seen in control adults
2. To determine whether a lower proportion of the final faecal samples from probiotic-receiving than from control subjects yields carbapenemase-bearing K pneumoniae on culture

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/03/2019, North West - Greater Manchester Central Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; Tel: +44 (0)207 104 8007; Email: nrescommittee.northwest-gmcentral@nhs.net), REC ref: 18/NW/0863

Study design
Randomised open-label feasibility study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Patients with colonised carbapenemase-bearing Klebsiella pneumoniae

Interventions
The intervention arm will involve patients taking the probiotic (as below). The control arm involves no intervention; there is no placebo so patients will be discharged without a supplement /probiotic.

The probiotic preparation to be used will be BioGaia Gastrus tablets (BioGaia AB, Stockholm, Sweden). BioGaia Gastrus chewable tablets is a dietary supplement containing a combination of the probiotic strain Lactobacillus reuteri 17938 (Lactobacillus reuteri Protectis) and Lactobacillus reuteri ATCC PTA 6475.

Dose: 1 chewable tablet per day for 21 days.

One tablet consists of a minimum of 200 million live Lactobacillus reuteri Gastrus. Ingredients: Bulking agent (isomalt), L. reuteri DSM 17938 and L. reuteri ATCC PTA 6475, fully hydrogenated vegetable oil (palm), flavour enhancer (ascorbic acid), mandarin flavouring and mint flavouring. One tablet consists of a minimum of 200 million live L. reuteri Gastrus. Net weight per tablet: 700 mg.

There is no physical follow-up visit at hospital. At 21 days patients will post a faecal sample to the hospital in a pre-paid sampling/postal kit. This will mark the end of trial involvement.

Intervention Type
Supplement

Primary outcome(s)
1. The feasibility of initiating studies in the secondary care setting, by identifying potential participants but study interventions carried out in the community
2. The feasibility of conducting a randomised controlled trial in immuno-competent adults known to be colonised with multi-resistant K pneumoniae and an assessment of recruitment and retention rates over a 12 month period

Key secondary outcome(s))
1. Faecal counts of multi-resistant Klebsiella pneumoniae measured using faecal sampling and culture at day 0 and day 21±2
2. Faecal counts of carbapenemase-bearing Klebsiella pneumoniae measured using faecal sampling and culture at day 0 and day 21±2

Completion date
17/12/2019

Eligibility

Key inclusion criteria
1. Written informed consent
2. Male or female; aged 18 years or older
3. Immunocompetent as per medical history
4. TCD-KP detected on rectal screening in the last 2 months
5. Not currently hospital inpatient (when planning starting probiotic supplementation)

All individuals will be considered for inclusion in this study regardless of age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion and belief, sex, and sexual orientation except where the study inclusion and exclusion criteria EXPLICITLY state otherwise.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any active infection at the time of enrolment
2. Presence of or likely to develop mucositis on examination, as per medical history
3. History of Presence cardiac prostheses
4. Consumption of any marketed probiotic product in the 30 day period prior to enrolment and during the duration of the trial
5. Consumption of Over the Counter (OTC) medication or herbal remedies labelled as to improve your immunity system or “for daily immunity”
6. In receipt of systemic or intestinal antibiotic within 14 days before baseline samples to be taken
7. Receiving or intended to receive antibiotic within 30 days of 1st baseline sample
8. Current and past history of pancreatitis
9. Concurrent melaena
10. Abdominal surgery within the 3 months prior to study enrolment
11. Known pericardial constriction, genetic hypertrophic cardiomyopathy, or infiltrative cardiomyopathy
12. Any medical condition, which in the opinion of the Investigator, may place the patient at higher risk from his/her participation in the study, or is likely to prevent the patient from complying with the requirements of the study or completing the study
13. Past medical history of Severe renal dysfunction at Visit 0, defined as e GFR <30 mL/min, or end-stage renal disease requiring dialysis.
14. History of severe hepatic impairment or liver dysfunction at Visit 0, defined as total bilirubin above the ULN (excluding patients with Gilbert’s syndrome), AST or ALT >3 times the ULN or alkaline phosphatase >2.5 times the ULN
15. Known hypersensitivity to any of the components of the probiotic.
16. Pregnancy, lactation or planning pregnancy. A pregnancy test will not be required before study enrolment, however, if a woman determines that she is pregnant during the study period, she must stop the probiotic

Date of first enrolment
02/09/2019

Date of final enrolment
26/11/2019

Locations

Countries of recruitment
United Kingdom

England

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

Study participating centre
Wythenshawe Hospital
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Sponsor information

Organisation
Manchester University NHS Foundation Trust

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Other

Funder Name
Healthcare Infection Society

Alternative Name(s)
The Healthcare Infection Society (HIS), Healthcare Infection Society (HIS), HIS

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No