ISRCTN70235902 https://doi.org/10.1186/ISRCTN70235902

Does oral colistin (antibiotic) eradicate extensively drug-resistant bacteria (Klebsiella) from the gastrointestinal tract?

Submission date
11/01/2023

Recruitment status
No longer recruiting

Registration date
12/01/2023

Overall study status
Completed

Last Edited
25/09/2023

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
Infections caused by carbapenem-resistant Klebsiella pneumoniae (CRKP) bacteria are common, difficult to treat with extremely limited antimicrobial options, and are associated with high death rates. These infections present an everyday clinical challenge to patients and their families, physicians, and health systems alike.
Decolonization therapy (DT) using oral non-absorbable colistin (an antibiotic) might be useful as a tool for preventing invasive bloodstream infections by CRKP in high-risk situations such as in intensive care, high dependency, and hematology units. The exact benefits and potential risks of oral colistin use are largely unknown.
This study aims to examine the impact of short-term use of oral colistin on the eradication of CRKP and the prevention of invasive bloodstream infection by this organism. The purpose is to investigate whether oral colistin eradicates Klebsiella from the gastrointestinal tract and whether this impacts the risk of invasive bloodstream infection by this organism.

Who can participate?
Patients aged 18 years and over admitted to intensive care, high dependency, and hematology wards at Sultan Qaboos University Hospital (Oman) during the study period who are colonised with CRKP (colistin susceptible)

What does the study involve?
This study will be conducted during the participants' hospitalization. The participants' discharge from the hospital shall not be affected by the study.
The treatment approach being investigated in this study differs from the standard treatment offered in this institution which is a “no decolonization strategy”. Participants will be given oral colistin or placebo four times per day for 7 days. Rectal swabs will be performed on day 7 after the end of treatment or placebo.

What are the possible benefits and risks of participating?
This study aims to further medical knowledge and may improve future strategies to prevent invasive disease by this difficult-to-treat bacterium. This research intervention may also directly

benefit the participants but it is not known for certain at this point. Potential risks include hypersensitivity to colistin and possibly gastrointestinal side effects such as nausea, vomiting, diarrhea, and abdominal pain, and the development of colistin resistance.

Where is the study run from?
Sultan Qaboos University Hospital (Oman)

When is the study starting and how long is it expected to run for?
July 2022 to September 2024

Who is funding the study?
Sultan Qaboos University (Oman)

Who is the main contact?
Dr Abdullah Balkhair, balkhair2020@gmail.com

Contact information

Type(s)
Principal investigator

Contact name
Dr Abdullah A Balkhair

ORCID ID
https://orcid.org/0000-0001-6911-5568

Contact details
Mazoun Street Al hail South
Muscat
Oman
111
+968 (0)243404
balkhair2020@gmail.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IG/MED/MEDE/23/03

Study information

Scientific Title

Eradication of carbapenem-resistant Klebsiella pneumoniae gastrointestinal colonization and prevention of secondary bloodstream infections with oral colistin

Acronym
CRKP-ColDT

Study objectives
This study aims to examine the impact of decolonization therapy (DT) using oral colistin on the eradication of CRKP (carbapenem-resistant Klebsiella pneumoniae) and the prevention of invasive bloodstream infection by this organism. It is hypothesized that oral colistin will result in a reduction in carriage, attributable and all-cause mortality, and incidence of invasive infection caused by CRKP.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/11/2022, Medical Research Ethics Committee (MREC) College of Medicine & Health Science, Sultan Qaboos University (PO Box 35, Al Khodh, 123, Oman; +968 (0)24143427; mrec@squ.edu.om), ref: SQU-EC/232/2022, MREC #2918

Study design
Double-blind placebo-controlled trial with balanced (1:1) randomization

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Eradication of carbapenem-resistant Klebsiella pneumoniae gastrointestinal colonization and prevention of invasive bloodstream infection by this organism

Interventions
Current intervention as of 09/05/2023:
Active screening of eligible patients for gastrointestinal colonization with CRKP will be performed by way of rectal swabs according to the hospital's standard operation procedures.

Eligible patients with a positive screening rectal swab for CRKP (colistin susceptible) and who are able to provide informed consent will be randomized by single sequence simple randomization to one of two arms:

Intervention arm:
Selective gastrointestinal decolonization with oral colistin [dose: 2 million units QID for 7 days].

Placebo [control] arm:
5 ml of sterile water for injection preparation QID for 7 days

Patients in both arms will be assessed at baseline and on day 7 after the end of treatment. At each time point, rectal swabs will be performed. The pre-defined primary outcome of the study was the detection of gastrointestinal CRKP carriage by a rectal swab at day 7 post-treatment (rate of eradication of CRKP at day 7 post-treatment). CRKP bacteremia, CRKP attributable death, and change in colistin MICs between baseline and day 7 after end of treatment will be assessed.

_____

Previous intervention:
Active screening of eligible patients for gastrointestinal colonization with CRKP will be performed by way of rectal swabs according to the hospital's standard operation procedures.

Eligible patients with a positive screening rectal swab for CRKP (colistin susceptible) and who are able to provide informed consent will be randomized by single sequence simple randomization to one of two arms:

Intervention arm:
Selective gastrointestinal decolonization with oral colistin [dose: 2 million units QID for 7 days].

Standard of care [control] arm:
No interventions (“watch and wait” strategy).

Patients in both arms will be assessed at baseline, on the last day of treatment (day 7), on days 14 and 28 after the end of treatment, and subsequent admissions within 6 months (when applicable). At each time point, rectal swabs will be performed. The pre-defined primary outcome of the study was the detection of gastrointestinal CRKP carriage by a rectal swab during day 28 post-treatment (rate of eradication of CRKP at day 28 post-treatment). CRKP bacteremia, CRKP-attributable death, and change in colistin minimal inhibitory concentrations (MICs) between baseline and day 28 after the end of treatment will be assessed.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Colistin (colistin sulphate) for oral use

Primary outcome(s)
Current primary outcome measure as of 09/05/2023:
CRKP eradication: Eradication [clearance] rate of CS-CRKP assessed by culture positivity of rectal swabs for CRKP at day 14 [day 7 post Rx]

_____

Previous primary outcome measures:
1. Eradication of CRKP assessed by culture positivity of rectal swabs for CRKP at day 28 post-intervention
2. CRKP bloodstream infection (bacteremia) assessed by blood culture for 28 days post-intervention

3. CRKP-related death will be captured by active follow-up of patients in both groups during hospitalization and for 28 days, whichever is longer

Key secondary outcome(s))
Current secondary outcome measure as of 09/05/2023:
1. Incidence of CS-CRKP bacteremia during the same hospitalization
2. In-hospital all-cause mortality during the same hospitalization
3. Incidence of colistin resistance in positive rectal swabs at day 14 [day 7 post Rx]

———

Previous secondary outcome measures:
Development of resistance to colistin evaluated by performing susceptibility testing of colistin for all post-intervention CRKP isolates from any site for 28 days

Completion date
30/09/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 09/05/2023:
1. Adult: Aged >18 years
2. Location: ICU, HD, Hematology
3. Able to provide informed consent
4. Expected to stay for 14 days in hospital
5. Undergone a screening rectal swab for CRKP within 72 h of admission

———

Previous inclusion criteria:
1. Aged ≥18 years
2. Admitted to intensive care, high dependency, and hematology wards at SQUH, Oman during the study period
3. Positive screening rectal swab for CRKP [colistin susceptible]
4. Able to provide informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

Current exclusion criteria as of 09/05/2023:
1. Not meeting inclusion criteria
2. Rectal swab is negative for CRKP
3. CRKP is colistin-resistant [MIC >2 mg/L)
4. Pregnant or nursing women
5. Known hypersensitivity to colistin/placebo
6. NPO [nil by mouth]
7. On colistin OR ceftazidime-avibactam/aztreonam at time of enrollment or up to 7 days before enrollment

———

Previous exclusion criteria:
1. Age <18 years
2. Pregnant or nursing women
3. Known hypersensitivity
4. Gastrointestinal colonization with colistin-resistant Klebsiella pneumonia
5. Enrollment in the present study for a previous episode

Date of first enrolment
15/10/2023

Date of final enrolment
30/04/2024

Locations

Countries of recruitment
Oman

Study participating centre
Sultan Qaboos University Hospital
PO Box 35, PC 123, Al Khod
Muscat
Oman
123

Sponsor information

Organisation
Sultan Qaboos University

ROR
https://ror.org/04wq8zb47

Funder(s)

Funder type
University/education

Funder Name
Sultan Qaboos University Project Code: IG/MED/MEDE/23/03

Alternative Name(s)
SQU

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Oman

Results and Publications

Individual participant data (IPD) sharing plan
The dataset will be made available upon request from the principal investigator Dr Abdullah Balkhair (balkhair2020@gmail.com).
The type of data that will be shared: Report of the board of data monitoring and any other essential data requested.
Dates of availability: Recruitment end date.
Whether consent from participants was required and obtained: Yes, a written consent is required and shall be obtained.
Comments on data anonymization: All data is anonymous
Any ethical or legal restrictions: None to the best of my knowledge
Any additional comments: None

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other files	Consent form		12/01/2023	No	No
Other files	Withdrawal of consent form		12/01/2023	No	No
Other files	Consent form version 3		03/04/2023	No	No
Participant information sheet			12/01/2023	No	Yes

Participant information sheet	version 2	03/04/2023	No	Yes