ISRCTN40310490 https://doi.org/10.1186/ISRCTN40310490

A paediatric intensive care study comparing the use of non-absorbable antibiotics and standard infection control to prevent secondary infection in critically ill children

Submission date
14/10/2020

Recruitment status
No longer recruiting

Registration date
30/10/2020

Overall study status
Completed

Last Edited
01/03/2024

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Each year, around 20,000 children are admitted to paediatric intensive care units (PICUs) in the UK. Critically ill children are at a higher risk of hospital-acquired infections. Many of these infections are caused by ‘bad’ bacteria in the digestive tract, such as those in the mouth and stomach. Normally there are higher levels of ‘good’ bacteria in the digestive tract. When someone is very poorly, the number of ‘bad’ bacteria may rise and spread to other organs. This can then cause severe illnesses, such as pneumonia and sepsis, and lead to long-term health problems, increased hospital costs and even death.

All PICUs have several methods to reduce the risk of hospital-acquired infections, such as providing antibacterial gel on units. One possible method is to treat patients with antibiotics that stop the growth of bacteria in the digestive tract. This treatment is called selective decontamination of the digestive tract (SDD). It has been shown in adults to reduce the number of hospital-acquired infections and improve survival. However, it is unclear if it works in children.

As large clinical trials are expensive, it is important to be confident that a trial can be done and that the different components of the trial can all work together. Before embarking on a full trial, we will conduct an 18-month feasibility study including a pilot trial. A feasibility study is a piece of research done before the main trial to answer the question “Can this trial be done?” and is used to estimate important factors such as willingness of patients to take part. A pilot trial is a miniature version of the full trial and is done to check that the different components, such as recruiting patients, delivering treatment and follow-up, all run smoothly.

Our aim is to compare giving SDD with not giving SDD (usual care) in children admitted to an NHS PICU. We also need to be sure that if SDD is used, it does not lead to a rise in resistance to antibiotics either in the patient or in the whole community

Who can participate?
A child can participate in the study if they are admitted to one of the 6 PICUs taking part in the trial and are expected to be on a breathing machine for at least 48 hours. We plan to include up to 324 patients and estimate 90 will receive SDD.

This study will also involve conducting interviews with parents of participating children to understand whether the study was acceptable to them, review how they were approached and the information provided, and what outcome measures are most important to them.

What does the study involve?
Six PICUs will be randomly assigned to either deliver, or not, SDD to eligible patients. All PICUs will start off not delivering SDD. Then halfway through, 3 of the PICUs will switch to delivering SDD. This type of study is known as a cluster randomised controlled trial. It ensures that the two groups of units, and the patients in those units, are as similar as possible, except for the delivery and receipt of SDD. It therefore allows us to see whether SDD is any more or less beneficial than the usual care given in the NHS. We will also monitor levels of antibiotic resistant bacteria in all participating PICUs by taking swabs from patients.

SDD is a mixture of antibiotic and antifungal in paste and liquid forms given in the following ways:
• A pea-sized amount of paste in your child's mouth
• 0.5 - 2 teaspoons of liquid through their feeding tube
This is done four times a day until the child no longer needs help from the ventilator.

What are the possible benefits and risks of participating?
SDD a treatment that can be used to reduce the number of bacteria within the gut which prevents any "bad" bacteria moving to other organs and causing serious infections. There are very few risks to a child from taking part. SDD has been in use for more than 30 years and is routine practice in many hospitals. The paste can taste a little bitter but will stop being used once the child is no longer ventilated.

Where is the study run from?
Intensive Care National Audit & Research Centre (UK)

When is the study starting and how long is it expected to run for?
April 2020 to October 2022

Who is funding the study?
National Institute for Health Research (NIHR) (UK) Health Technology Assessment (HTA) Programme (project number: 16/152/01)

Who is the main contact?
Dr Nazima Pathan, np409@medschl.cam.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Nazima Pathan

ORCID ID
https://orcid.org/0000-0002-9447-4252

Contact details
Department of Paediatrics
University of Cambridge
Level 8, Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ
+44 (0)20 7269 9277
picnic@icnarc.org

Additional identifiers

Integrated Research Application System (IRAS)
239324

Central Portfolio Management System (CPMS)
44969

Study information

Scientific Title
A pilot cluster randomised clinical trial of the use of selective gut decontamination in critically ill children: Paediatric Intensive Care and Infection Control (PICnIC)

Acronym
PICnIC

Study objectives
PICniC is a feasibility study designed to determine whether it is possible to conduct a cluster randomised trial (cRCT) of Selective Decontamination of the Digestive tract (SDD) in critically ill children who are likely to be ventilated for >48 hours, and to explore and test the acceptability of key components of the study to healthcare professionals and families of patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/09/2020, West Midlands – Black Country Research and Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8010; blackcountry.rec@hra.nhs.uk), ref: 20/WM/0061

Primary study design
Interventional

Study design

Interventional cluster randomized case controlled study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Digestive tract infection in critically ill children

Interventions
The PICnIC study is a pilot, parallel group cluster randomised clinical trial (cRCT) that includes an integrated mixed methods study. We will discuss the cRCT and mixed-methods separately. The whole study has designed as a miniature version of a potential definitive cRCT and will test feasibility and the study procedures.

cRCT
Participating sites will undergo an 8-week baseline period of usual care, during which sites will be randomised to either continuing usual care (control) or delivering SDD (intervention) in the second 8-week period. There will be a 2-week transition period between the delivery of usual care and starting the intervention. The trial is unblinded, SDD will become usual practice for participating PICUs randomised to deliver the intervention.

There will be three 1-week observational ecological assessments over the course of the study: pre-trial; during the transition period; post-trial.

Eligible patients will be:
1. AgeD >37 weeks (corrected gestational age) and <16 years
2. Receiving mechanical ventilation expected to last at least 48 h (and expected to remain so until the day after tomorrow)
All patients admitted to the study PICU during the ecological surveillance weeks will be included, regardless of their ventilation status.

The intervention will be started in all eligible patients as it will form part of the standard infection control strategy in the participating PICU. In addition to usual care, the follow SDD regimen will be adopted:
1. A 6-hourly topical, application of a pea-sized (0.5 g) amount of paste to the mouth
2. A 6-hourly administration of liquid given via the existing feeding tube into the stomach via the nose. The amount of liquid given will vary based on the child's age between half a teaspoon – 2 teaspoons (2.5 – 10 ml)
Treatment will be given 30 minutes before feeds, where feeding is not continuous. This dosing regimen is based on that in use in a UK PICU for a period of over 10 years. The intervention will start in all eligible patients within 6 h of the child fulfilling the inclusion criteria. It will continue until the patient is extubated or for 30 days, whichever is sooner.

Readmitted patients will continue to receive the intervention, as it will form part of the standard care bundle but would not be counted as a separate enrolment.

Per standard practice, routine surveillance swabs will be taken from all patients on admission. Additional surveillance swabs will then be taken twice-weekly until discharge (or on the day of discharge for admission durations less than 7 days). Samples taken will be:
1. Respiratory
2. Urine

3. Stool or rectal
4. Wound (where present)

Data collection will be restricted to data required to address the objectives. Where possible, data will be obtained from standard data collection via PICAnet to maximise efficiency. A number of additional data points will be collected to inform possible outcomes for a definitive trial (duration of invasive mechanical ventilation, days alive and free of mechanical ventilation censored at 30 days, infectious episodes during PICU admission, total antibiotic usage in PICU, duration of PICU stay and hospital stay, mortality at PICU discharge and 30 days post-randomisation).
Adverse events will be monitored and reported up to 30 days post-randomisation.

Mixed Methods study
Health Care Professionals
All health care professionals currently working in a UK PICU will be invited to take part in an online survey. Additionally, focus groups will be held with healthcare professionals from two of the participating PICUs, with opportunities for telephone interviews for those unable to attend the group.
These will explore health care professionals' views on:
• acceptability of the trial design including selection of, and adherence to, the SDD intervention;
• acceptability of recruitment and deferred consent procedures in the trial; and
• acceptability of the overall trial procedures.

Parents/Guardians
The parents/guardians of each recruited child will be asked to complete a short, anonymous questionnaire which will seek their experiences of:
• recruitment and emergency consent;
• content and format of the PIS;
• decision-making in the PICU setting; and
• acceptability of the overall trial procedures.

Parents/guardians will also be invited to take part in a more detailed telephone interview. Interviews will be completed until data saturation (anticipated to be 15-25 based on previous studies).

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Colistin, tobramycin, nystatin

Primary outcome(s)
Feasibility outcomes:
1. Adherence to the SDD intervention assessed by the proportion of eligible children allocated to the intervention that receive SDD using case report forms
2. Estimation of recruitment rate measured using ...
3. Questionnaires and interviews will be used to explore parents/legal representatives' views on: the acceptability of conducting a definitive trial; the content and understanding of the

information materials; acceptability of the recruitment and consenting procedures; and the selection of important, relevant, patient-centred, primary and secondary outcomes for a definitive trial.
4. Two focus groups and up to 10 interviews with practitioners involved in the pilot cRCT, as well as an online survey of all UK PICU staff will be used to assess: the acceptability of the implementation of the SDD intervention; interest in participation in a definitive trial in the wider PICU community; the acceptability of the recruitment and consenting procedures for the definitive trial; and the acceptability of collecting data for assessing the selected clinical and ecological outcomes

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
31/10/2022

Eligibility

Key inclusion criteria
Pilot cRCT:
1. Aged >37 weeks (corrected gestational age) and <16 years
2. Receiving mechanical ventilation expected to last at least 48 h (and expected to remain so until the day after tomorrow)

Mixed methods study:
3. Online survey/telephone interviews: All health care professionals working in a PICU within the UK
4. Focus Groups: All healthcare professionals working in the two PICUs selected for focus groups
5. Survey/telephone interviews: Parents/legal representatives of all recruited patients

Participant type(s)
Patient, Health professional

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
37 Weeks

Upper age limit
16 Years

Sex
All

Total final enrolment
361

Key exclusion criteria
1. Known allergy, sensitivity or interaction to polymyxin E, tobramycin, or nystatin
2. Known to be pregnant
3. Death perceived as imminent

Date of first enrolment
20/09/2021

Date of final enrolment
13/02/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Addenbrookes Hosital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Birmingham Children's Hospital
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
John Radcliffe Hopsital
Headley Way
Oxford
United Kingdom
OX3 9DU

Study participating centre
Southampton General Hospital
Tremona Road
Southampton

United Kingdom
SO16 6YD

Study participating centre
Bristol Royal Hospital for Children
Upper Maudlin Street
Bristol
United Kingdom
BS2 8BJ

Study participating centre
St. Georges Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 16/152/01

Funder Name
National Institute for Health Research (NIHR) (UK)

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 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?
Results article		07/12/2023	11/12/2023	Yes	No
Results article		01/02/2024	01/03/2024	Yes	No
Protocol article		11/03/2022	14/03/2022	Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes