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Fever pilot trial

Submission date
31/07/2017

Recruitment status
No longer recruiting

Registration date
14/08/2017

Overall study status
Completed

Last Edited
20/09/2023

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
A fever (high temperature) is a normal response by the body to infection. When a very sick child has a fever, the usual reaction from clinicians (doctors/nurses) is to cool down the child. This can be done using drugs, such as paracetamol, using a cooling mat or sponging the child with water. The temperature at which clinicians usually start these treatments is about 37.5°C. There is strong evidence, however, that fever may be an important bodily response and may actually help a child to recover from infection. In 2013, the National Institute for Health and Care Excellence (NICE) updated guidance for managing fever in children. It recommended that drugs should not be used only for the purpose of reducing a child's temperature. Most of the evidence for this recommendation came from research in non-critically ill children, therefore, it is unknown whether this recommendation should be applied to very sick children. The aim of this study is to compare giving treatments for fever at a higher temperature than usual, such as 39.5°C, with the usual temperature of around 37.5°C in children with infection admitted to an NHS paediatric intensive care unit (PICU). This is a small study to find out whether it is possible to perform a larger study to determine the effects of the current practice of strict control of fever with a more permissive approach. As large studies are expensive, it is important to be confident that this study can be done and that the different parts can work together. This study is the third part of an 18-month feasibility study. A feasibility study is research done before a full study to answer the question "can this trial be done?" It is used to estimate important factors such as willingness of parents/children to take part. The first part of this feasibility study (which has now completed) involved conducting interviews with parents/legal guardians to understand whether the proposed study is acceptable to them. Views were discussed on using deferred consent, as this study and the proposed bigger study will incorporate a deferred consent process. Deferred consent is an approach which has successfully been used in previous emergency/critical care studies and involves including a child in a study without prior consent from their parents /guardians and then seeking agreement later. The second part (which has almost completed) involved observing and collecting data on children with fever from infection in 22 PICUs to tell us how many children would need to take part in a full study and which are the best outcomes to use.

Who can participate?
Children aged under 16 with a confirmed or suspected infection causing a fever, admitted to PICU in four NHS hospitals

What does the study involve?
Participants are randomly allocated to either a permissive approach to fever management (starting drugs/cooling methods to control temperature once they reach a temperature of >39.5° C), or a restrictive approach (starting drugs/cooling methods to control temperature at ≥37.5°C). Telephone interviews/questionnaires are conducted with parents/legal representatives of the recruited participants, and focus groups/questionnaires with staff in the research sites. This is to further understand the feasibility of the consent and study procedures for the potential larger study.

What are the possible benefits and risks of participating?
There is the possibility of a beneficial effect from the permissive treatment, therefore it is not considered as carrying any significant risk, but rather carrying a potential benefit. The patients not receiving permissive treatment receive usual care and are not prone to unknown risk either. Young children may have seizures during a fever, but reducing a fever does not reduce this risk. The seizures are likely to be caused by the infection that the fever is trying to help the body heal. Another possible risk is that a high temperature uses extra energy and can make the heart beat more quickly. Patients receiving permissive treatment are therefore closely monitored.

Where is the study run from?
1. Great Ormond Street Hospital (UK)
2. Alder Hey Children's NHS Foundation Trust (UK)
3. Evelina London Children's Hospital (UK)
4. Great North Children's Hospital (UK)

When is the study starting and how long is it expected to run for?
April 2017 to March 2018

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

Who is the main contact?
1. Dr Imran Khan
fever@icnarc.org
2. Prof. Mark Peters
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Study website
https://www.icnarc.org/Our-Research/Studies/Fever

Contact information

Type(s)
Public

Contact name
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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
34598

Study information

Scientific Title
A multi-centre randomised, parallel group pilot clinical trial investigating the feasibility of a definitive trial of a permissive temperature strategy in critically ill children with known or suspected infection

Study objectives
The aim of this study is to assess the feasibility of a trial comparing a permissive approach to fever (treat at ≥39.5 degC) with a standard restrictive approach (treat at >37.5 degC).

Ethics approval required
Old ethics approval format

Ethics approval(s)
London – Hampstead Research Ethics Committee, 11/08/2017, ref: 17/LO/1139

Study design

Randomised; Interventional; Design type: Process of Care, Management of Care

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Specialty: Children, Primary sub-specialty: Allergy, Infection and Immunity ; UKCRC code/ Disease: Infection/ Other viral diseases

Interventions
Current interventions as of 04/05/2018:
The trial incorporates a pragmatic approach to temperature control in both the permissive group and restrictive group.
Permissive group: Treatments to reduce temperature are only permitted in response to a temperature at or above 39.5°C while mechanically ventilated.
Restrictive group: Treatments to reduce temperature are permitted in response to a temperature at or above 37.5°C while mechanically ventilated.
The treatment strategies for the restrictive and permissive group will commence from randomisation until PICU discharge or death.

Previous interventions:
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Restrictive group: Treatments to reduce temperature are permitted in response to a temperature at or above 37.5°C.
The treatment strategies for the restrictive and permissive group will commence from randomisation until PICU discharge or death.

Intervention Type
Other

Primary outcome measure
Number of eligible patients recruited per site, per month is measured using the proportion of eligible children recorded in trial screening logs that were recruited to the Fever Pilot Trial at baseline

Secondary outcome measures
1. Proportion of parents/legal representatives refusing deferred consent is measured as the proportion of recruited children whose parents subsequently declined to give consent or who withdrew their child from the Fever Pilot Trial having initially given consent through study complete (an average of 24 hours)
2. The acceptability of the information and documentation and of the consenting procedures is measured using the survey responses from parents who gave and declined to give consent; and qualitative evaluation of telephone interview transcripts from interviews with parents who gave and declined to give consent at study complete (an average of 24 hours)
3. Adherence to the selected temperature thresholds for antipyretic intervention in both the higher temperature threshold (intervention) and standard care groups is measured as the proportion of time spent below the allocated threshold; and
the proportion of children that received antipyretic intervention on days when their maximum temperature did not reach the allocated threshold; and the proportion of children that did not receive antipyretic intervention on days when their maximum temperature exceeded the allocated threshold at six hourly observations of temperature and antipyretic use over the first seven days as well as daily maximum peak temperature until 28 days.
4. Separation between the randomised groups in peak temperature measurement over the first 48 hours following randomisation is assessed as the difference in the mean of the maximum temperature recorded during the first 48 hours following randomisation between the higher temperature threshold and standard care groups, presented with a 95% confidence interval at baseline
5. Length of ventilation and Length of PICU stay is measured as the proportion of randomised patients with outcome available in each group, mean (standard deviation) in each group, median and quartiles in each group at study completion (an average 2 days)
6. PICU mortality is measured as the proportion of randomised patients with outcome available in each group
number (percentage) in each group through study completion (an average 2 days)
7. Days of organ specific support is measured as proportion of randomised patients with outcome available in each group
through study completion (an average 2 days)

Overall study start date
03/04/2017

Completion date
13/04/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/05/2018:
1. Unplanned PICU admission
2. Age ≥ 28 days and < 16 years
3. Referral requiring PICU admission to a participating unit
4. Fever ≥ 37.5°C in the first 48 hours following contact with the paediatric retrieval service/PICU
5. New requirement for mechanical ventilation
6. Treating clinician presumes the cause of the fever is an infective process

Previous inclusion criteria:
1. Unplanned PICU admission

2. Age ≥ 28 days and < 16 years
3. Referral requiring PICU admission to a participating unit
4. Fever ≥ 37.5°C in the first 48 hours following contact with the paediatric retrieval service/PICU
5. Receiving or requiring mechanical ventilation
6. Treating clinician presumes the cause of the fever is an infective process

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 205; UK Sample Size: 205

Key exclusion criteria
Current exclusion criteria as of 04/05/2018:
1. Acute encephalopathy, including convulsive status epilepticus
2. Post-cardiopulmonary bypass or known/suspected cardiomyopathy/myocarditis
3. Rhabdomyolysis
4. Malignant hyperthermia, neuroleptic malignant syndrome or drug-induced hyperthermia
5. Receiving palliative care or death perceived as imminent
6. Previously recruited to the Fever Pilot Trial

Previous exclusion criteria:
1. Acute encephalopathy, including convulsive status epilepticus
2. Post-cardiopulmonary bypass or known/suspected cardiomyopathy/myocarditis
3. Severe rhabdomyolysis
4. Sickle cell disease
5. Malignant hyperthermia, neuroleptic malignant syndrome or drug-induced hyperthermia
6. Receiving palliative care or death perceived as imminent

Date of first enrolment
01/10/2017

Date of final enrolment
31/01/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Great Ormond Street Hospital
Great Ormond Street Hospital for Children NHS Foundation Trust
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
Alder Hey Children's NHS Foundation Trust
Eaton Road
Liverpool
United Kingdom
L12 2AP

Study participating centre
Evelina London Children's Hospital
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Great North Children's Hospital
Victoria Wing
Royal Victoria Infirmary
Newcastle upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation
Intensive Care National Audit And Research Centre (ICNARC)

Sponsor details
Napier House
24 High Holborn
London

England
United Kingdom
WC1V 6AZ

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/057b2ek35

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

Publication and dissemination plan
A report will be submitted to the NIHR HTA Programme for publication in Health Technology Assessment – deadline 31 March 2018

The findings will also be published in appropriate peer-reviewed scientific journals and relevant professional journals 6 months after trial end date.

The results of the Fever feasibility study will be disseminated to patients and their families via the Clinical Studies Group for Children (Anaesthesia, Critical Care and Cardiology) soon after the NIHR-HTA report publication.

Intention to publish date

31/03/2018

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?
Results article	results	01/02/2019	25/02/2019	Yes	No
Protocol article		15/06/2022	12/08/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article	Permissive versus restrictive temperature thresholds	07/03/2019	20/09/2023	Yes	No
Results article	acceptability findings	10/03/2021	20/09/2023	Yes	No