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A randomised controlled trial of a procalcitonin-based algorithm to guide antibiotic use in acute pancreatitis

Submission date
20/12/2017

Recruitment status
No longer recruiting

Registration date
07/02/2018

Overall study status
Completed

Last Edited
22/07/2022

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
The pancreas is an organ in the upper abdomen sitting below the stomach. Its function is to produce enzymes to digest food, as well as producing hormones to control blood sugars. When the pancreas becomes inflamed it can cause pain and sickness, as well as affecting other vital organs. This condition is termed acute pancreatitis. The severity of acute pancreatitis can range from being mild to very severe where some patients spend a long time in hospital. Acute pancreatitis is treated mainly by rehydration, as well as giving pain relief and anti-sickness medications. The inflammation usually settles on its own. However, for the small minority of patients who are unfortunate to develop a severe form of acute pancreatitis, bacterial infection around the pancreas can be a problem, and this may require additional treatment such as antibiotics. Telling the difference between inflammation and bacterial infection in acute pancreatitis can be difficult. Both conditions can cause a fever and a fast heart rate. Antibiotics are often prescribed where there is no bacterial infection, so there will be no benefit to patients, but can cause harmful side-effects such as severe diarrhea and inflammation of the bowel. There is also a risk of developing bacteria that are resistant to common antibiotics, limiting the choice of antibiotics if they are needed in the future. It is therefore important to only give antibiotics to those patients who have a bacterial infection. There are blood tests, such as Procalcitonin, that can help to distinguish between inflammation and infection. The aim of this study is to see how effective Procalcitonin is at guiding doctors in using antibiotics in acute pancreatitis.
Procalcitonin is produced by the cells in our body in response to infection. This can be measured in blood samples. At the moment, it can be used to guide antibiotic treatment in common conditions such as chest infections. Its role for patients with acute pancreatitis who are suspected of having infection, however, is not yet clear.

Who can participate?
Patients aged over 18 with acute pancreatitis

What does the study involve?
Participants are randomly allocated to receive antibiotics either in response to a procalcitonin algorithm or by standard decision making. All other aspects of the care of patients are the same.

The study assesses whether the use of procalcitonin measurement allows for a reduction in the use of antibiotics without compromising patient outcome.

What are the possible benefits and risks of participating?
There is evidence from other studies that the use of procalcitonin measurement to guide antibiotic use results in more appropriate use of antibiotics. There are not likely to be any risks from participation.

Where is the study run from?
Manchester Royal Infirmary (UK)

When is the study starting and how long is it expected to run for?
January 2017 to December 2020
The study opened to recruitment on the 26th July 2018 and will recruit for two years

Who is funding the study?
Manchester University NHS Foundation Trust (UK)

Who is the main contact?
Prof. Ajith Siriwardena

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Version 1.0

Study information

Scientific Title
PROCalcitonin-based algorithm for antibiotic use in Acute Pancreatitis: a randomised controlled trial

Acronym
PROCAP

Study objectives
This study tests the hypothesis that a procalcitonin-based algorithm to guide initiation, continuation and discontinuation of antibiotics will lead to reduced antibiotic use in patients with acute pancreatitis without an adverse effect on outcome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/04/2018, North West - Haydock Research Ethics Committee (3rd Floor - Barlow House, 4 Minshull Street, Manchester, M1 3DZ; Tel: +44 (0)207 104 8012; Email: nrescommittee.northwest-haydock@nhs.net), REC ref: 18/NW/0255

Study design
Single-centre randomised controlled single-blind two-arm phase III pragmatic clinical and cost-effectiveness trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

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

Health condition(s) or problem(s) studied
Acute pancreatitis

Interventions
Method of randomisation:
Web-based randomisation will be provided by the Clinical Trials Unit of the University of Edinburgh (https://www.ed.ac.uk/usher/edinburgh-clinical-trials). Allocation will be in a ratio of 1:1 to routine or algorithm-guided care. Randomization will be stratified by severity (mild or

moderately severe/severe) and admission pathway (whether or not the patient has their index (first) admission with acute pancreatitis to the Manchester Royal Infirmary [direct] or is transferred from another hospital [tertiary transfer]). A random block size of 4, 6 or 8 will be applied to each stratum.

Patients will be randomly allocated to receive antibiotics either in response to a procalcitonin algorithm or by standard decision making. All other aspects of the care of patients will be the same. The main endpoint is whether the use of procalcitonin measurement allows for a reduction in use of antibiotics without compromising outcome.

Summary methodology for intervention arm:
The intervention is the use of a procalcitonin-based algorithm to guide antibiotic use. The algorithm is a simplified, bi-modal guide: consider antibiotic use if PCT >1 ng/mL, do not use if PCT below this point. Patients will undergo baseline and follow-up sampling of PCT. In addition, PCT should be measured if there is a clinical suspicion of infection or if antibiotic use is being considered. Where possible, antibiotic use should be commenced with appropriate support from the PCT algorithm and discontinued in compliance with repeat PCT measurement.
All care of patients with acute pancreatitis in the intervention arm will be standard with the sole exception of antibiotic use which will be guided by the PCT algorithm.

Summary methodology in the control arm:
All care of patients with acute pancreatitis in the control arm will be standard.

Duration of treatment:
Patients will remain within the study for 90 days or until discharge from hospital (if later).

Follow-up:
Patients will be followed for 90 days or until discharge from hospital (if later).

Intervention Type
Other

Primary outcome measure
Current primary outcome measure as of 25/03/2020:
Whether antibiotic use is initiated during the index stay. Trial antibiotic use will exclude mandated routine antibiotic use, specifically prophylaxis before procedures such as laparoscopic cholecystectomy or ERCP.
Antibiotics prescribed before the index admission (from the referring hospital or community) will be recorded at admission but not included in the primary endpoint.

Previous primary outcome measure:
Days of antibiotic use, defined as any day (24 hour period) when antibiotics were prescribed on the patient's drug prescription chart and administered. This will be recorded as days of antibiotic use until the 90th day or until discharge from hospital (if later).

Secondary outcome measures
All secondary outcomes measured as occurring up to the 90th day or until discharge from hospital (if later):
1. Clinical infections as defined according to the centers for disease control
2. New isolates of multi-resistant bacteria (Clostridium difficile, vancomycin resistant enterococcus [VRE], methicillin resistant staphylococcus aureus [MRSA], carbapenemase

producing enterobacteriaceae [CPE])
3. Incidence of multi-resistant organism bacteraemia
4. Infection of pancreatic necrosis, defined either as a result of fine needle aspiration (FNA), radiological evidence of gas in a peri-pancreatic collection or positive microbiological cultures from surgical or post-mortem specimens
5. Use of radiological, endoscopic or surgical intervention
6. Length of inpatient stay (by level of care: critical care levels II/III, ward-based care)
7. Re-admission to hospital within 6 weeks of onset of index episode
8. Episode-related mortality and cause
9. Quality of life, assessed by the EQ-5D-5L questionnaire
10. Cost analysis from an NHS perspective, including inpatient resource use

Overall study start date
03/01/2017

Completion date
31/12/2020

Eligibility

Key inclusion criteria
Adult patients presenting with acute pancreatitis admitted or referred to the service. Inclusion criteria include:
1. Patients over the age of 18 years of age
2. Ability to provide informed consent
3. The diagnosis of acute pancreatitis requires two of the following three features:
3.1. Abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back)
3.2. Serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal
3.3. Characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging (MRI) or transabdominal ultrasonography

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
260

Total final enrolment
260

Key exclusion criteria
1. Patients under the age of 18 years of age
2. Patients who are unable to give informed consent (criterion removed 14/06/2019)
3. Infectious conditions requiring prolonged antibiotic therapy – such as infective endocarditis
4. Severely immunocompromised patients – such as those with human immunodeficiency virus and with a CD4 count of less than 200 cells/mm3; neutropenic patients (<500 neutrophils/mm3)
5. Patients on immunosuppressive therapy
6. Previous thyroid surgery

Date of first enrolment
26/07/2018

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Manchester Royal Infirmary
Oxford Road
Manchester
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M13 9WL

Sponsor information

Organisation
Manchester University NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Manchester University NHS Foundation Trust

Results and Publications

Publication and dissemination plan
It is the trialists' intention to publish the protocol in a peer-reviewed journal. It has not currently been submitted. Clinical and economic analysis will be conducted to a prospective analysis plan made available to journal referees. The results will be presented at appropriate national and international meetings. The results will be published regardless of the final results of the trial.

Intention to publish date
05/10/2021

Individual participant data (IPD) sharing plan
The participant-level data that will be recorded for this study are highly specific to the PROCAP analysis and should not be used for unspecified secondary analyses. Therefore the trialists do not plan to make these data available. The primary data will be stored as paper-based case report forms in a locked office in the Manchester Royal Infirmary.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	29/07/2019	31/07/2019	Yes	No
Protocol file	version v3.0	24/03/2020	26/03/2020	No	No
Results article		18/07/2022	22/07/2022	Yes	No
HRA research summary			28/06/2023	No	No