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A randomised controlled trial of single antibiotic cement versus dual antibiotic cement in patients receiving a partial hip joint replacement after fracture

Submission date
16/07/2018

Recruitment status
No longer recruiting

Registration date
17/07/2018

Overall study status
Completed

Last Edited
26/06/2023

Condition category
Surgery

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

Plain English summary of protocol

Background and study aims
This study is comparing two types of treatments in patients who have suffered a hip fracture and need to have a partial hip replacement (also called a hemiarthroplasty). The hemiarthroplasty implant is inserted into the thigh bone and replaces the 'ball' part of the 'ball-and-socket' hip joint. 'Bone cement' is used to hold the implant in place. This study aims to compare two different antibiotic bone cement mixtures used to hold the implant in place. The results of this trial should show whether there is any difference in the rate of deep infection in patients when one of the two bone cement mixtures is used to hold their hemiarthroplasty implant in place. The information gained will help patients and their doctors make more informed decisions about the best way to reduce the risk of deep infection in this type of surgery.

Who can participate?
Patients 60 years of age or older who have been admitted to a participating hospital with a hip fracture that the surgeon feels should be treated with a hip hemiarthroplasty

What does the study involve?
Participants are randomly allocated to receive one of two types of bone cement. The first type has a lower dose of a single type of antibiotic, and the second type has a higher dose of that same antibiotic, as well as a second type of antibiotic. Participants complete a questionnaire about their recovery by telephone at 120 days after their surgery.

What are the possible benefits and risks of participating?
There is no specific advantage to patients from taking part in the study. However, the results of this study will help to decide which treatment is best for patients with this type of injury. Any operation for a broken hip carries some risks. The risks of surgery with an implant include: bleeding requiring blood transfusion, infection, further fracture, dislocation, leg length discrepancy, blood clots, damage to nerves and blood vessels in the surgical area, and the risks

associated with the anaesthetic. These risks are the same as for patients who are not part of this study. There are also uncommon risks associated with both types of cement. In a small number of cases, patients having a cemented replacement can have a reaction to the bone cement. If this were to occur, the anaesthetist and surgeon would continue treatment as per normal practice. This risk is the same for both types of bone cement.

Where is the study run from?
The study is sponsored by the Northumbria Healthcare NHS Foundation Trust and is managed by Oxford Trauma, a clinical trials research group which is a part of the Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS) at the University of Oxford. There will be 20+ hospitals from across the United Kingdom participating in the study.

When is the study starting and how long is it expected to run for?
December 2017 to December 2021

Who is funding the study?
Heraeus Medical GmbH

Who is the main contact?
Stephanie Wallis
white8-copal@ndorms.ox.ac.uk

Study website
https://white8.octru.ox.ac.uk/

Contact information

Type(s)
Scientific

Contact name
Ms Stephanie Wallis

Contact details
Northumbria Healthcare NHS Foundation Trust
Woodhorn Lane
Ashington
United Kingdom
NE63 9JJ
+44 (0)1865 223111
White8-copal@ndorms.ox.ac.uk

Type(s)
Scientific

Contact name
Prof Mike Reed

Contact details
Northumbria Healthcare NHS Foundation Trust
Woodhorn Lane

Ashington
United Kingdom
NE63 9JJ

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
38386

Study information

Scientific Title
WHiTE 8 COPAL: a randomised controlled trial of low dose single antibiotic loaded cement versus high dose dual antibiotic loaded cement in patients receiving a hip hemiarthroplasty after fracture

Acronym
WHiTE 8 COPAL

Study objectives
This trial aims to establish if a high dose, dual antibiotic regime has fewer infections compared to low dose single antibiotic cement.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales REC 5, 03/05/2018, ref: 18/WA/0154

Study design
Randomised; Interventional; Design type: Treatment, Surgery

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 to request a patient information sheet

Health condition(s) or problem(s) studied
Hip fracture

Interventions
Participants will undergo surgery at the next available opportunity on a planned trauma list. Participants will be blinded to the treatment allocation. The operating surgeon will not be blinded to the allocation. Where possible clinical outcomes will be assessed by blinded assessors. Patients will be kept blinded until the completion of the trial when the blind may be broken.

Group 1: Cemented hemiarthroplasty with low dose single antibiotic cement
Replacement of the femoral head and neck with choice of femoral head and stem. Cement used will be Heraeus Palacos R+G cement (Hanau, Germany) – contains gentamicin 0.5 grams per 40 gram mix of cement.

Group 2: Cemented hemiarthroplasty with high dose dual antibiotic cement
Replacement of the femoral head and neck with choice of femoral head and stem. Cement used will be Heraeus Copal G+C cement (Hanau, Germany) – contains gentamicin 1 g and clindamycin 1 g per 40 gram mix of cement.

Following fixation all patients will undergo a routine rehabilitation prior to discharge from hospital. Research staff will complete the infection-related questions at baseline, and at 4 months (120 days) post-surgery. In addition the following data will be collected:
1. Demographic and baseline characteristics (e.g. age, gender, pre-fracture mobility)
2. Routine 'operation notes' and 'discharge summaries' that include details of patient's diagnosis and treatment, perioperative complications, and discharge details
3. Medical record review for diagnosis of infection
4. Details of admission, assessment and treatment
5. Details of antibiotics use and microbiological reports for reported infections
6. Contact details, including of carers when appropriate
7. Complications and SAEs during the study period

Following their 4-month questionnaire, patients will have completed their participation in the trial and will continue to be treated as per normal standard of care.

Intervention Type
Procedure/Surgery

Primary outcome measure
Deep Infection of surgical wound; the trialists will use the Centre for Disease Control and Prevention definition of a “deep surgical site infection”, that is a wound infection involving the tissues deep to the skin that occurs within 90 days of injury. Medical records for all patients will be reviewed by appropriately trained staff for indicators of infection at the time of the patient’s discharge from the research site. In addition, at 120 days post-surgery, the patients will self-report (via telephone interview, electronic media or postal questionnaire) on signs of infections. When potential signs of infection have been found, either at discharge or 120 days, the site will be asked to provide, if available, copies of: any re-operation records for surgery related to the

index hip fracture, details of antibiotics prescribed, microbiology reports if samples of the suspected infected tissues around the hip were sent for analysis and imaging reports for any deep imaging that occurred in relation to suspected infection. These data will be collated by the central trial team in Oxford.

Secondary outcome measures
1. Mortality recorded at discharge from the research site as well as in the 120-day follow-up. Sites or consultees may also report mortality at any point in the time between discharge and 120 days.
2. Health-related quality of life measured by EuroQol EQ-5D-5L at baseline and at 120 days post-surgery
3. All complications and surgical interventions related to the index wound will be recorded. These are reported by sites as they become aware of events, as well as by patients, carers or consultees at 4 months (120 days)
4. Antibiotic prescription information will be obtained from the patient, consultee or carer at the 4 months (120 days) follow-up. Should the patient be entered into the trial under nominated consultee agreement and this information not be available from a carer, the trial team may contact the patient's GP for this information
5. Resistance patterns of infections; all infections identified in the primary endpoint will be assessed for antibiotic resistance profiles by the local microbiology team
6. Resource use; cost data will be obtained from national databases or will be estimated in consultation with the hospital finance department. The cost consequences following discharge, including NHS costs and patients' out-of-pocket expenses will be recorded via a short questionnaire, which will be administered at 4 months (120 days) post-surgery. This will be either by patient or consultee
7. Mobility; the ability to walk indoors and outdoors is rated very highly by patients. It has been included in a recommended 'core outcome set' for trials assessing interventions in hip fractures, hence it will be recorded using the CRF. It will be captured at baseline and at 4 months (120 days).
8. Residential status; also captured on CRF. The residential status is also part of the core outcome set for hip fractures and NHFD dataset. It will be captured at baseline and at 4 months (120 days)

Overall study start date
15/12/2017

Completion date
31/12/2021

Eligibility

Key inclusion criteria
1. Aged 60 years or older
2. Intracapsular hip fracture, which in the opinion of the treating surgeon requires acute surgical treatment with a cemented hip hemiarthroplasty

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
Planned Sample Size: 4920; UK Sample Size: 4920

Total final enrolment
4936

Key exclusion criteria
Patients will be excluded if they are allergic to gentamicin or clindamycin

Date of first enrolment
01/08/2018

Date of final enrolment
31/08/2021

Locations

Countries of recruitment
England

United Kingdom

United States of America

Wales

Study participating centre
John Radcliffe Hospital
Oxford
United Kingdom
OX3 9DU

Study participating centre
Leicester Royal Infirmary
Musculoskeletal Research Office
Ground Floor, Victoria Building
Leicester
United Kingdom
LE1 5WW

Study participating centre

Norfolk & Norwich University Hospital
Orthopaedic Research
East Block Level 2
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Poole Hospital
Research Dept
Cornelia House
Longfleet Road
Poole
United Kingdom
BH15 2JB

Study participating centre
Queen Alexandra Hospital
ED Research Team
Lancaster House
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Queen Elizabeth Hospital
NIHR SRMRC
4th Floor
North Block
Institute of Translational Medicine
Hertiage Building
Birmingham
United Kingdom
B15 2TH

Study participating centre
Royal Berkshire Hospital
Research and Development
Level 2 | North Block
London Road

Reading
United Kingdom
RG1 5AN

Study participating centre
Princess Royal Hospital
Research & Development
Sussex House
1 Abbey Road
Brighton
United Kingdom
BN12 1ES

Study participating centre
Royal Victoria Infirmary
Peacock Hall
Level 2, Room 12
Newcastle Upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Southmead Hospital
Trauma & Orthopaedic Research Team
Department of Orthopaedics
Office 6, Gate 18, Level 1
Brunel Building
Bristol
United Kingdom
BS10 5NB

Study participating centre
University Hospital Coventry
Trauma & Orthopaedic Research Team
Research & Development
Room ACF40002
4th Floor, West Wing
UHCW, Clifford Bridge Road
Walsgrave
Coventry
United Kingdom
CV2 2DX

Study participating centre
Queens Medical Centre
T & O Research Manager
Trauma & Orthopaedic Audit Office
C Floor, West Block, QMC (WC1285)
Nottingham University Hospitals
Nottingham
United Kingdom
NG7 2UH

Study participating centre
University Hospital Wales
Trauma & Orthopaedics Directorate
Cardiff & Vale University Health Board
Cardiff & Vale Orthopaedic Centre (CAVOC)
University Hospital Llandough
Penlan Road
Penarth
Cardiff
United Kingdom
CF64 2XX

Study participating centre
University Hospital Aintree
John Moorehead
Orthopaedic Research Room
Fracture Clinic
Lower Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre
Salford Royal Hospital
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre

Morriston Hospital
Heol Maes Eglwys
Morriston
United Kingdom
SA6 6NL

Study participating centre
Wythenshawe Hospital
University Hospital of South Manchester
Southmoor Road
Wythenshawe
United States of America
M23 9LT

Study participating centre
Blackpool Victoria Hospital
Clinical Research Centre
2nd Flor, Area 5
Whinney Heys Road
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Ipswich Hospital
The East Suffolk North Essex NHS Foundation Trust
Heath Road
Ipswich
United Kingdom
IP4 5PD

Study participating centre
James Cook University Hospital
Academic Centre
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre

Sandwell General Hospital
Sandwell & West Birmingham Hospitals NHS Trust
Sandwell Medical Research Unit
Opposite Diabetes Centre
Lyndon
West Bromwich
United Kingdom
B71 4HJ

Study participating centre
Royal Cornwall Hospital
Medical & Surgical Research Team
B16 Knowledge Spa
Royal Cornwall Hospitals NHS Trust
Truro
United Kingdom
TR1 3HD

Study participating centre
Northumbria Specialist Emergency Care Hospital
Wansbeck General Hospital
Woodhorn Lane
Ashington
United Kingdom
NE63 9JJ

Study participating centre
Kings College Hospital
Orthopaedic Department
2nd Floor, Hambleden Wing
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Horton General Hospital
Oxford Road
Banbury
United Kingdom
OX16 9AL

Sponsor information

Organisation
Northumbria Healthcare NHS Foundation Trust

Sponsor details
North Tyneside General Hospital
Rake Lane, North Shields
Tyne & Wear
North Shields
England
United Kingdom
NE29 8NH
+44 (0)344 811 8111
white8-copal@ndorms.ox.ac.uk

Sponsor type
Hospital/treatment centre

Website
https://www.northumbria.nhs.uk/

ROR
https://ror.org/01gfeyd95

Funder(s)

Funder type
Industry

Funder Name
Heraeus Medical GmbH

Results and Publications

Publication and dissemination plan
Protocol will be published after the start of the trial. Planned publication of the results in a high-impact peer reviewed journal.

Intention to publish date
01/05/2023

Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		01/02/2021	14/04/2021	Yes	No
Results article		21/06/2023	26/06/2023	Yes	No
HRA research summary			28/06/2023	No	No