ISRCTN10817487 https://doi.org/10.1186/ISRCTN10817487

World Hip Trauma Evaluation - LIT: an investigation in people 60 years and over with a hip fracture to determine whether an infusion of a local anaesthetic (lidocaine) can reduce symptoms of delirium in the first five days after hip fracture surgery

Submission date
11/06/2021

Recruitment status
Recruiting

Registration date
19/01/2022

Overall study status
Ongoing

Last Edited
22/10/2024

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English Summary
Background and study aims
This study has been designed following a James Lind Alliance Patient and Public Research Priority Setting Partnership, which identified the following question as a top research priority: “What are the best treatments to prevent and treat confusion and delirium after surgery in adults with a broken bone in the leg?” The study has been co-produced with the UK Musculoskeletal Trauma Patient and Public Involvement Group.

A broken hip (hip fracture) is a very serious injury that requires surgery to repair or replace the broken bone followed by a long period in hospital to recover. Around a quarter of patients with hip fracture die within a year and those that survive have a permanent loss of their quality of life. Worldwide there are 1.3 million hip fractures each year, with more than 70,000 in the UK.

Around a quarter of patients who have a hip fracture have an episode of ‘delirium’ after their surgery. Delirium is a condition where the patient loses awareness of themselves and their environment, and has difficulty thinking clearly. For relatives and friends, as well as the patient, delirium is very disturbing. The symptoms of delirium are similar to those of patients with dementia but develop over a short period and tend to vary over time. The great majority of patients suffering with delirium recover quite quickly, but delirium leads to longer hospital stays and a greater risk of complications. Delirium is also associated with an increased risk of developing dementia in later life.

Inflammation, caused by the hip fracture and by the surgery to repair the hip, is thought to be the root cause of delirium. This study will investigate the use of a drug called ‘lidocaine’ to see if it reduces the risk of delirium after surgery for a hip fracture. Lidocaine is already used very

widely in the NHS as a local anaesthetic, but it also has a strong anti-inflammatory effect. If lidocaine is given to a patient during surgery to reduce inflammation, it may reduce the severity of delirium after surgery.

Who can participate?
This study falls under the WHITE Platform framework and is open to all patients aged over 60 years with a hip fracture, apart from the very small number of patients who have an allergy or another reason not to have lidocaine. Eligible patients will be approached about the study before their treatment where possible. Patients who are unable to consent for themselves may take part in the trial with the agreement of their relatives or an independent doctor, who will be known as legal representatives.

What does the study involve?
Patients from at least 12 hospitals in the UK will be approached to take part in the study. 416 participants will take part. Half will be allocated by chance to a slow injection of lidocaine during their surgery, and half to a placebo injection containing no lidocaine. Neither the patients nor their doctors will know which treatment they had to make the study fair. All other elements of the patients' treatment will follow the normal care pathway for all hip fracture patients at the hospital.

We will use a series of simple questions to measure symptoms of delirium in the first five days after surgery. We will also assess the patients' mobility, quality of life and complications and review if they develop symptoms of dementia in the 12 months after surgery. We will also work out the cost of the treatment – for the individual, for the health service and in terms of social support in the year following the fracture. We will also ask people for their permission to monitor their long-term health outcome from national databases that are already being routinely collected. Any information collected from these databases will not contain any details which could identify the patient.

What are the possible benefits and risks of participating?
The risks of hip surgery include infection, blood clots, chest or urine infection - these risks are the same as for people who are not part of this research project.
The risks associated with intravenous lidocaine include minor symptoms such as tingling of the lips. More serious effects such as disturbances of heart rhythm can occur but are very unlikely at the doses used in this treatment comparison. Patients will have continuous monitoring whilst the lidocaine is being given, and an emergency treatment to reverse these effects is available. Lidocaine has been used safely like this in other types of surgery for many years.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
May 2020 to December 2026

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

Who is the main contact?
Katy Mironov
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Contact information

Type(s)
Scientific

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Public

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Additional identifiers

EudraCT/CTIS number
2020-003719-83

IRAS number
287755

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 287755, CPMS 49156, NIHR201943

Study information

Scientific Title
World Hip Trauma Evaluation - LIT: Lidocaine Intravenous Trial

Acronym
WHITE 10-LIT

Study hypothesis
To establish if there are differences in peak delirium in the 5 days following hip fracture surgery between hip fracture patients receiving a peri-operative lidocaine infusion or a saline placebo infusion.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/01/2021, Berkshire Research Ethics Committee (Berkshire South Central REC, Easthampstead Baptist Church, Southill Road, Bracknell, RG12 7NS, UK; +44 (0)2071048138; berkshire.rec@hra.nhs.uk), ref: 20/SC/0452

Study design
Pragmatic multicentre two-arm randomized superiority comparison with parallel economic analyses follow-up

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

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

Condition
Hip fracture

Interventions
WHiTE 10-LIT is a randomised comparison appended to the World Hip Trauma Evaluation (WHiTE) Platform. WHiTE is a platform trials framework, designed to efficiently deliver multiple randomised comparisons of interventions for patients aged 60 years and over with a hip fracture. The platform and its appended randomised comparisons are governed by one single

set of ethical and regulatory approvals and an explicit legal basis and processing purpose for the use of patient-level data. The Platform affords a common core dataset and documentation.

Individual randomised comparisons are not dependent on each other and each will have its unique start and stop dates and publication of results without compromising the integrity of the platform.

Participants will be randomised on a 1:1 basis to lidocaine or placebo infusion, stratified by presence of cognitive impairment at presentation and recruitment centre:
1. Intervention: Intravenous lidocaine 1.5 mg.kg-1 bolus followed by infusion of 1.5 mg.kg-1.h-1 for the duration of surgery
2. Placebo control: Identical volumes of 0.9% saline

The allowed maximum absolute dose will be 120 mg and 120 mg h-1 regardless of weight.

Randomisation will be on a 1:1 basis to lidocaine or placebo, stratified by the presence/absence of permanent cognitive impairment at presentation and recruitment centre. The allocation sequence will be generated by the trial statistician using variable block sizes and stored securely in a web-based encrypted system provided by the CTU.

An appropriately trained individual other than the treating clinician or anyone involved in the assessment of any trial outcomes will carry out the online randomisation and prepare a syringe with the allocated intervention, in an area away from the clinical team. The prepared syringe will then be labelled 'lidocaine 1% or saline 0.9%' so as not to reveal the treatment allocation to the treating anaesthetist when they administer it to the participant in order to ensure that the patient is not treated differently during the surgery. Lidocaine and saline are clear colourless solutions, indistinguishable to the human eye.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
lidocaine hydrochloride injection BP 1% w/v.

Primary outcome measure
Peak post-operative delirium as measured by the Memorial Delirium Assessment Scale (MDAS) at days 1-5 after surgery.

Secondary outcome measures
1. Pain measured using the standard Functional Pain Scale (FPS)/Pain Assessment in People with Advanced Dementia (PAINAD), for participants with and without mental capacity respectively, before surgery and days 1-5 after surgery.
2. Delirium screening using the 4AT test before surgery and days 1-5 after surgery.
3. Health-related quality of life using the Euroqol-5D-5L pre-injury, at 4 and 12 months post-diagnosis of a hip fracture.
4. Cognitive impairment using the Telephone Interview for Cognitive Status (TICS) at 4 and 12 months post-diagnosis of a hip fracture.
5. Subjective mobility status measured using the UK National Hip Fracture Database Mobility

Scale at 4 and 12 months post-diagnosis of a hip fracture
6. Residential status measured using the UK National Hip Fracture Database Residential Status at 4 and 12 months post-diagnosis of a hip fracture
7. Mortality risk using death notification up to 12 months post-diagnosis of a hip fracture
8. Risk and pattern of complications measured using bespoke reporting forms up to 12 months post-diagnosis of a hip fracture.
9. Resource use from an NHS and personal social services perspective calculated using bespoke reporting forms up to 12 months post-diagnosis of a hip fracture.

Overall study start date
01/05/2020

Overall study end date
31/12/2026

Eligibility

Participant inclusion criteria
Platform inclusion criteria:
1. Aged ≥60 years
2. Diagnosed with a hip fracture that in the opinion of the treating surgeon may benefit from surgical treatment

No additional specific inclusion criteria for LIT.

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
416

Participant exclusion criteria
Platform exclusion criteria.
1. Previous participation in the same randomised comparison
2. A second hip fracture (other side) while the patient is still enrolled in the Platform following their first hip fracture

Additional specific exclusion criteria for LIT:
1. Body weight estimated to be <40 kg or >100 kg
2. Known subdural haematoma
3. Known allergy to local anaesthetics
4. Severely impaired renal (eGFR <30 ml.min-1) or hepatic (based on clinical history) function
5. Patient has specific contraindications to lidocaine:
5.1. All grades of atrioventricular block; severe myocardial depression; sino-atrial disorders

5.2. Acute porphyria
5. 3. Current congestive cardiac failure
6. Concurrent participation in a clinical trial of a medicinal product or recent participation within 5 half-lives of the last dose of medicinal product
7. Local anaesthetic nerve block administered within the previous 6 hours
8. Known serum albumin <30 g/l

Recruitment start date
31/01/2022

Recruitment end date
30/05/2025

Locations

Countries of recruitment
England

United Kingdom

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

Study participating centre
Queen's Medical Centre
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Cardiff ECMC
Cardiff University
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XN

Study participating centre

Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
Calderdale and Huddersfield NHS Foundation Trust
Trust Headquarters
Acre Street
Lindley
Huddersfield
United Kingdom
HD3 3EA

Study participating centre
Warwickshire North Cdc
George Eliot Hospital NHS Trust
College Street
Nuneaton
United Kingdom
CV10 7DJ

Study participating centre
Pinderfields Hospitals NHS Trust
Trust Hq, Rowan House
Pinderfields General Hospital
Aberford Road
Wakefield
United Kingdom
WF1 4EE

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

Study participating centre

Heartlands Hospital
Bordesley Green East
Bordesley Green
Birmingham
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B9 5ST

Study participating centre
NIHR Cambridge Biomedical Research Centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
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Study participating centre
Royal Liverpool University Hospital
Prescot Street
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Study participating centre
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Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

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

Funder Name
NIHR Oxford Biomedical Research Centre

Alternative Name(s)
NIHR Biomedical Research Centre, Oxford, OxBRC

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Protocol will be published before recruitment has been completed. The statistical analysis plan will be published before the final data has been collected. Main clinical results and health economic evaluation will be published in high impact peer-reviewed journals after completion of the initial 1 year follow-up period.

Intention to publish date
31/12/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the Lead Investigator (Prof Matt Costa matthew.costa@ndorms.ox.ac.uk). Each request will be reviewed and decided upon on a case-by-case basis. Participants will be informed via the Participant Information Sheet (and will consent to the contents of this PIS) of the possibility of de-identified datasets being made available following appropriate requests.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No