ISRCTN54191675 https://doi.org/10.1186/ISRCTN54191675

Liposomal bupivacaine in knee replacement surgery

Submission date
13/11/2017

Recruitment status
No longer recruiting

Registration date
14/11/2017

Overall study status
Completed

Last Edited
28/11/2024

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
At the moment, in the UK, a local anaesthetic (a medication that numbs an area of the body) called bupivacaine hydrochloride is routinely used during knee replacement surgery. This drug is injected around the knee at the time of surgery to help reduce the levels of pain experienced afterwards. There is a new local anaesthetic called liposomal bupivacaine (also known as Exparel) that has been used routinely in the USA since 2011. Using Exparel will help to reduce the level of pain experienced after surgery, but it is thought that the pain relief may be felt for longer. The aim of this study is to compare these two local anaesthetic injections against each other, and show whether or not there is an extended period of pain relief when Exparel is used as well as to see if using Exparel reduces the need for other types of pain relief post-operation. This study will also look at the cost of using Exparel, and whether it would be a cost-effective alternative to the current treatment.

Who can participate?
Adults aged 18 and older who have end stage osteoarthritis of the knee.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive the liposomal bupivacaine. Those in the second group receive the bupivacaine. The surgical team performing the operation administers the drug via wound infiltration during surgery. After the operation, the patient will be cared for as per routine care at the hospital. For 3 days (72 hours) after the surgery, the patient will be asked to complete a daily questionnaire so that the study team can find out how they are feeling after the surgery. Participants are asked about their recovery throughout hospitalisation and at six weeks, six months and one year postoperatively.

What are the possible benefits and risks of participating?
Whilst Exparel is not currently used routinely in the United Kingdom, it has been used in the United States since 2011 and the safety profile has been reviewed both independently and with the UK regulators (Medicines and Healthcare products Regulatory Agency) prior to this trial.
The main benefit of taking part will be the information the researchers get from this study which will help them assess how patients do after receiving this anaesthetic. This will improve treatment of future patients with knee osteoarthritis. There are no anticipated risks or

disadvantages to participating in SPAARK. The operation will be performed by an experienced and trained Consultant Surgeon. There are risks associated with all surgery and anaesthetics. Steps are always taken to ensure that these risks are minimised. As part of routine care, the patient will be well informed of potential risks. Participating in this study will not affect the standard of care received. The most common side effects of Exparel administration are nausea, constipation and vomiting. These are also side effects associated with having a general anaesthetic for an operation. Most patients (9 out of 10) do not experience these side effects.

Where is the study run from?
This study is being run by the Surgical Intervention Trials Unit (SITU) at the University of Oxford (UK).

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

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

Who is the main contact?
SITU-NDORMS, situ@ndorms.ox.ac.uk

Contact information

Type(s)
Public

Contact name
Dr . SITU-NDORMS team

Contact details
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Additional identifiers

EudraCT/CTIS number
2016-003154-32

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
32227

Study information

Scientific Title
Study of Peri-Articular Anaesthetic for Replacement of the Knee. The clinical and cost effectiveness of peri-articular liposomal bupivacaine compared with bupivacaine hydrochloride for post-operative recovery after knee replacement surgery: A multi-centre, blinded, randomised controlled trial

Acronym
SPAARK

Study objectives
This study aims to evaluate the effectiveness of liposomal bupivacaine versus standard bupivacaine on post-operative recovery for total knee replacement patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford C Research Ethics Committee, 19/07/2017, ref: 17/SC/0139

Study design
Randomised; Interventional; Design type: Treatment, Drug, 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
Elective orthopaedic surgery

Interventions
Patients with osteoarthritis of the knee that require a knee replacement operation are asked to take part in the study. During the clinic appointment, the surgeon tells the patient a little bit about the study and the local research nurses discuss the study and what it involves. This should

take about 10 minutes. If the patient is interested in participating, they are assessed by one of the research team to answer some questions about their knee function and are asked to complete a questionnaire. The researcher also examines the knee. During the knee operation, as part of the routine operation, the surgeon injects local anaesthetic around the knee. If a patient consents to participate they are randomly assigned to receive either the current local anaesthetic injection (bupivacaine hydrochloride) or the new trial local anaesthetic injection (liposomal bupivacaine). Both injections are given using the same technique before the surgeon finishes the operation. After the operation, the patient will be cared for as per routine care at the hospital. For 3 days (72 hours) after the surgery, the participant are asked to complete a daily questionnaire so that the study team can find out how they are feeling after the surgery. Routine hospital follow-up for this operation is at approximately six weeks and six months post-surgery. The SPAARK assessments are scheduled at the same time so that the participants do not have to make an extra 'research only' visit to the hospital. Ahead of these appointments, the participants are sent a questionnaire to complete and return (either by post or email). A questionnaire is also sent one year after the operation. This should take about half an hour to complete.

Allocation to either local anaesthetic is done randomly as this is the best way to allow a fair comparison to be made between the two treatments. This is the standard and only reliable way to see how good a treatment is. Whichever local anaesthetic is allocated, the patient will still be under the care of their surgeon and their professional clinical team. The patient does not know which local anaesthetic they receive as SPAARK is a "blinded" trial. The surgeon knows which medication the patient is allocated to, but for the purposes of the study, the patient is not be told. The reason for this is to stop the patient's questionnaire answers from being influenced by which medication they were allocated. This information is kept confidential unless there is a problem.

Intervention Type
Other

Phase
Phase III

Primary outcome measure
The effectiveness of liposomal bupivacaine with bupivacaine hydrochloride compared to bupivacaine hydrochloride alone on post-operative recovery is assessed both in terms of systemic recovery as well as local recovery of the operated joint. This will be measured using the quality of recovery 40 Score at 72 hours and the cumulative daily pain score at rest using VAS 0 to 72 hours.

Secondary outcome measures
1. Other markers of recovery both in the short term and long term are measured using:
1.1. Mean pain score measured using a 0-10 VAS at: baseline and evening of surgery day 0, 1, 2 and 3 following surgery
1.2. Quality of Recovery 40 Score at baseline and evening of surgery day 0, 1, 2 and 3 following surgery
1.3. Cumulative opioid consumption over 72 hours.
1.4. Fitness for discharge against pre-defined criteria at evening of surgery day 0, 1, 2 and 3 following surgery
1.5. Functional outcome at baseline, 6 weeks, 6 months and 1 year (Oxford Knee Score, American Knee Society Score)

2. Cost effectiveness of the intervention compared with the current standard of care is measured using cost utility analysis using patient-reported quality of life as the main outcome, obtained using the EuroQol EQ-5D-5L questionnaire at baseline, 72 hours, 6 weeks, 6 months and 1 year
3. Safety is measured using serious adverse events, specifically cardiovascular or wound complications within 30 days of surgery

Overall study start date
01/04/2017

Completion date
28/02/2021

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 11/01/2019:
1. Unilateral primary knee replacement, including both total knee replacement (TKR) and unicompartmental knee replacement (UKR), for end-stage osteoarthritis
2. American Society of Anaesthesiologists (ASA) Grade I to III
3. Participant is willing and able to consent for themselves
4. Male or female, aged 18 years or above
5. In the Investigator's opinion, is able and willing to comply with all trial requirements

Previous participant inclusion criteria as of 26/10/2018:
1. Unilateral primary knee replacement, including both total knee replacement (TKR) or unicompartmental knee replacement (UKR), for end stage osteoarthritis
2. Willing and able consent for themselves
3. Male or female, aged 18 years or above
4. In the Investigator's opinion, is able and willing to comply with all trial requirements.

Previous participant inclusion criteria:
1. Participant is willing and able consent for themselves
2. Male or Female, aged 18 years or above
3. End stage osteoarthritis of the knee
4. In the Investigator's opinion, is able and willing to comply with all trial requirements

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

Planned Sample Size: 500; UK Sample Size: 500

Total final enrolment
533

Key exclusion criteria
Current participant exclusion criteria as of 11/01/2019:
1. Allergy or intolerance to amide-type local anaesthetics
2. Objective evidence of nerve damage in the affected lower limb
3. Rheumatoid arthritis
4. Any other significant disease, disorder or condition which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the results of the trial, or the participant's ability to participate in the trial
5. Participants who have participated in another research trial involving an investigational product in the past 6 months
6. Participants who have significant cognitive impairment or language issues
7. Contra-lateral knee replacement within the trial or within 12 months prior to randomization

Previous participant exclusion criteria as of 26/10/2018:
1. American Society of Anaesthesiologists (ASA) Grade III or above
2. Allergy or intolerance to amide type local anaesthetics
3. Objective evidence of nerve damage in the affected lower limb
4. Rheumatoid arthritis
5. Any other significant disease, disorder or condition which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the results of the trial, or the participant's ability to participate in the trial
6. Participants who have participated in another research trial involving an investigational product in the past 6 months
7. Participants who have significant cognitive impairment or language issues
8. Contra-lateral knee replacement within the trial or within 12 months prior to randomisation

Previous participant exclusion criteria:
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4. Rheumatoid arthritis
5. Any other significant disease, disorder or condition which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial.
6. Participants who have participated in another research trial involving an investigational product in the past 6 months
7. Participants who have significant cognitive impairment or language issues
8. Contra-lateral knee replacement (If the patient is receiving staged bilateral knees, they may still participate in the trial but data will only be included from the first knee)

Date of first enrolment
27/11/2017

Date of final enrolment
29/02/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Chapel Allerton Hospital
Chapeltown Road
Leeds
United Kingdom
LS7 4SA

Study participating centre
Pinderfields Hospital
Aberford Road
Wakefield
United Kingdom
WF1 4DG

Study participating centre
Rotherham General Hospital
Moorgate Road
Rotherham
United Kingdom
S60 2UD

Study participating centre
The Robert Jones and Agnes Hunt Orthopaedic Hospital
Gobowen
Oswestry
United Kingdom
SY10 7AG

Study participating centre
Torbay Hospital
Lowes Bridge
Torquay
United Kingdom
TQ2 7AA

Study participating centre
The Whittington Hospital
Magdala Ave
London
United Kingdom
N19 5NF

Study participating centre
Pilgrim Hospital
Sibsey Road
Boston
United Kingdom
PE21 9QS

Study participating centre
Yeovil District Hospital
Higher Kingston
Yeovil
United Kingdom
BA21 4AT

Study participating centre
King's Mill Hospital
Mansfield Road
Sutton-in-Ashfield
United Kingdom
NG17 4JL

Sponsor information

Organisation
University of Leeds

Sponsor details
Joint Leeds Sponsor Office
Research & Innovation
34 Hyde Terrace
Leeds
England

United Kingdom
LS2 9LN

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/024mrxd33

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
Results of this trial will be submitted for publication in a peerreviewed journal. All presentations and publications will be preagreed by the Trial Steering Committee (TSC).

Intention to publish date
31/08/2021

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?
Protocol article	protocol	16/12/2019	18/12/2019	Yes	No
Statistical Analysis Plan	statistical analysis plan	17/05/2021	19/05/2021	No	No
Results article		06/04/2022	07/04/2022	Yes	No
HRA research summary			28/06/2023	No	No