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The role of soluble epoxide hydrolase in osteoarthritis pain

Submission date
27/02/2025

Recruitment status
Recruiting

Registration date
21/03/2025

Overall study status
Ongoing

Last Edited
07/03/2025

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Osteoarthritis (OA) is a leading cause of pain and reduced mobility in the adult population. A protein called soluble epoxide hydrolase (sEH) could be very important in helping treat OA in the future. The sEH protein is responsible for breaking down anti-inflammatory and pain-relieving molecules called EETs into pro-inflammatory DHETs. This study aims to look at the relationship between levels of sEH in the knee joint with levels of these molecules in the blood and how much pain is felt.

Who can participate?
Patients aged over 40 years attending elective surgery clinical for knee replacement surgery due to osteoarthritis pain.

What does the study involve?
Pre-Surgery Visit:
This appointment will take around 1 hour. You will be given the opportunity to ask any questions you have about the study before being asked to sign a consent form. A range of assessments will be undertaken at this appointment. The assessments comprise answering some questions about the levels of pain you feel and performing some measures of your pain sensitivity. Ahead of your research visit, we will send you one questionnaire to complete at home and bring to your appointment. This questionnaire should take around 20-30 minutes to complete, the questionnaire can also be completed during the research visit and you can also use this time to ask any questions you have about the questionnaire. At the end of your research visit we will provide you with another short questionnaire which should take around 5 minutes to complete. Tea, coffee, water, and snacks will be available during your research visit.

Day of Surgery:
On the day you receive your surgery a researcher from the study will ask you three short questions about your current levels of pain. During surgery, the surgeon will perform the operation as normal and will also collect 20 ml of blood, synovial fluid from your knee joint, and joint tissue removed as part of the surgery (this would usually be discarded). A member of the research team will collect this tissue from the surgery team, and transfer this to secure storage at the Clinical Sciences Building.

Post-Surgery Visit:
Six months after your surgery, you will be invited to attend another research visit. This will involve the same tests and questionnaires as your pre-surgery visit, and we will also take a fasted blood sample (20 ml). Tea, coffee, water, and snacks will be available once we have collected the blood sample.

What are the possible benefits and risks of participating?
We do not expect the study to help you, although we do hope you will find it interesting. We expect that the information we get from this study will help improve treatment for people with knee pain in the future.
We appreciate that your participation will take some of your time and will try to minimise the inconvenience to you. Clinical assessments will cause some mild temporary pain that should not last for more than a few minutes. If during the clinical assessments, for any reason, you ask us to stop the procedure we will immediately stop. Although blood collection is a very safe procedure, it may cause mild discomfort and occasionally a small bruise, nausea, lightheadedness or fainting may occur. Blood collections will be performed by trained phlebotomists within Academic Rheumatology, Clinical Sciences Building, City Hospital, Hucknall Road, NG5 1PB.

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

When is the study starting and how long is it expected to run for?
November 2024 to October 2028

Who is funding the study?
This study is funded by the Medical Research Council (MR/Z506618/1) as part of the Project “Targeting the therapeutic potential of soluble epoxide hydrolase for the treatment of osteoarthritis pain”.

Who is the main contact?
Prof. Victoria Chapman, Victoria.Chapman@nottingham.ac.uk

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
333889

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
UoN: 25009

Study information

Scientific Title
Targeting the therapeutic potential of soluble epoxide hydrolase for the treatment of osteoarthritis pain

Acronym
HOPE

Study objectives

The effectiveness of soluble epoxide hydrolase (sEH) in breaking down the beneficial EET molecules into their inactive metabolites contributes to the amount of osteoarthritis (OA) pain people experience, providing an opportunity for new targeted treatments.

Ethics approval required
Ethics approval required

Ethics approval(s)
Not yet submitted, Ethics committee name not provided (Address not provided, City not provided, Zip/postal code not provided; Telephone number not provided; Email not provided), ref: Reference number not provided

Study design
Observational cross sectional study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Other

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

Health condition(s) or problem(s) studied
Osteoarthritis

Interventions
For the first research visit (up to 4 weeks pre-surgery) participants will receive two questionnaires through the post to complete and return upon their visit to Academic Rheumatology. These will take approximately 30 minutes to complete and may also be completed on-site if preferred. On this visit, participants will be invited to take part in some pain phenotyping measurements performed by a trained member of the research team, which are not invasive and cause temporary discomfort. First, participants will be weighed and measured in order to calculate their BMI. Pain pressure threshold will be performed on the leg and the arm, this involves applying pressure to the site using a probe, when the participant begins to feel pain they push a button, the test is stopped and the pressure is recorded. The pain phenotyping measurements will last no longer than 45 minutes. All the equipment is owned and maintained by the Pain Centre Versus Arthritis.

On the day of surgery, participants will be asked some brief questions on their current levels of pain and proceed with their surgery and care as normal. During the surgery, TK will collect samples of blood, synovial fluid, and joint tissue which was removed as part of the usual surgical procedure. Participants will be monitored following surgery as part of their routine care.

At the 6-month post-surgery follow-up visit the pain phenotyping measurement will be repeated, and a fasted blood sample (20 ml) collected. Research visits will take place in the morning, and participants offered their preferred time where possible. Venipuncture may cause some mild discomfort, and participants will be monitored for 20 minutes and provided with refreshments after the blood sample has been collected.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Pain is measured using the visual analogue score (VAS) and quantitative sensory testing (QST) at baseline and 6-months post-surgery
2. Levels of synovial inflammation measured using histopathology at baseline
3. sEH expression measured using nanobody assay at baseline
4. sEH activity measured using radiometric assay at baseline
5. Epoxyeicosatrienoic acids (EETs) and dihydroxyeicosatrienoic acids (DHETs) measured using liquid chromatography-mass spectrometry at baseline

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
01/11/2024

Completion date
31/10/2028

Eligibility

Key inclusion criteria
1. Adult patients who attend Nottingham University Hospitals for total knee replacement surgery as treatment for osteoarthritis pain
2. Able to give informed consent
3. No prior history of knee surgery
4. Aged over 40 years (no upper age limit)

Participant type(s)
Patient

Age group
Adult

Lower age limit
40 Years

Upper age limit
110 Years

Sex
Both

Target number of participants
120 (60 female and 60 male)

Key exclusion criteria
1. Also have symptomatic hip OA pain
2. Diagnosed with major psychiatric or neurological illness
3. Have active cancer
4. Have sensory dysfunction
5. Have other pain conditions, e.g. fibromyalgia
6. Currently using strong opioid or neuropathic treatments

Date of first enrolment
01/04/2025

Date of final enrolment
01/10/2027

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Nottingham University Hospitals NHS Trust - City Campus
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
University of Nottingham
University Park
Nottingham
United Kingdom
NG7 2RD

Sponsor information

Organisation
University of Nottingham

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E-Floor
Yang Fujia Building
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rfpd@mrc.ukri.org.uk

Sponsor type
University/education

Website
https://www.nottingham.ac.uk/research/ethics-and-integrity/#Researchethics

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The results of our research will be published as articles in peer-reviewed scientific journals, and they will be presented and discussed at international conferences. These are likely to be available around 1-2 years after recruitment has been completed. Participant's individual results will not be identifiable in any reports or publications.

An overall summary of research findings with links to further information will be given to patients who consent to their contact details being retained by the research team. This report will be co-developed by our patient advisory group

Intention to publish date
01/06/2028

Individual participant data (IPD) sharing plan
Participant's individual results will not be identifiable in any reports or publications.

IPD sharing plan summary
Stored in non-publicly available repository, Data sharing statement to be made available at a later date