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Investigating the influence of intravenous and oral tranexamic acid on blood loss for patients undergoing primary hip and knee replacements

Submission date
03/06/2016

Recruitment status
No longer recruiting

Registration date
21/06/2016

Overall study status
Completed

Last Edited
10/07/2023

Condition category
Musculoskeletal Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Patients having a hip or knee replacement lose almost a third of their blood during and after the operation. Many patients, especially those who are older will need a blood transfusion, suffer from anaemia (low levels of red cells in the blood) or have a slow recovery after the operation. Tranexamic acid is a medication used to treat or prevent excessive blood loss. It is used regularly in other areas of medicine, but only in patients who are likely to bleed a lot in routine hip or knee replacement surgery. In order to use this drug as in standard care for all patients, a study needs to be carried out to find out how well tranexamic acid works to reduce blood loss after the operation in a large group of patients having a hip or knee replacement, including those at risk of blood clots. This study also aims to find out how safe tranexamic acid treatment is to use in different patients and the best way to give tranexamic acid (in tablet form or through a drip), as well as how much to give and how long it should be given after an operation.

Who can participate?
Adults awaiting hip or knee replacement surgery.

What does the study involve?
Patients who are suitable and agree to take part are randomly placed in one of three treatment groups: no treatment (standard care), receiving treatment (tranexamic acid) during the hip or knee operation through a drip, or receiving treatment during the hip or knee operation through a drip plus taking a tablet every 8 hours (starting at 2 hours) for 24 hours after the operation. Patients are not evenly distributed among the three groups, as there will be a 1-in-5 chance of being in the no treatment group and a 2-in-5 chance of being in one of the treatment groups. For all patients, total blood loss is recorded 48 hours after surgery. A blood sample is also taken when the standard blood tests are done in order to measure how well the heart and blood clotting systems are working. For patients receiving treatment, if the routine kidney function tests taken before their operation show less than normal function, a lower does of tranexamic acid is used.

What are the possible benefits and risks of participating?
It is expected that patients who receive the tranexamic acid will benefit from losing much less blood during and after their operation, and so be less likely to need a blood transfusion, have reduced stress on the heart and have an easier recovery. Tranexamic acid can cause side effects like other drugs. Mild nausea, vomiting, diarrhoea and allergic reactions are rare but possible. The drug literature mentions that patients with a history of clots are at a higher risk of another clot when taking tranexamic acid. However no studies on tranexamic acid have ever found this to be true. Depending on the diagnosis, patients who have had a previous clot will be included because we think that these patients will benefit the most from reduced blood loss. In addition, in this study, patients will only take tranexamic acid for one day. For other conditions, patients safely take tranexamic acid for a number of days or weeks.

Where is the study run from?
Primary Joint Unit, Musgrave Park Hospital (UK)

When is study starting and how long is it expected to run for?
January 2016 to June 2019

Who is funding the study?
Belfast Arthroplasty Research Trust (UK)

Who is the main contact?
Professor David Beverland
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Contact information

Type(s)
Scientific

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-002661-36

Protocol serial number
15039DB-SW

Study information

Scientific Title
Single centre randomised controlled trial to assess the effect of the addition of twenty-four hours of oral tranexamic acid post-operatively to a single intra-operative intravenous dose of tranexamic acid on calculated blood loss following primary hip and knee arthroplasty

Acronym
TRAC-24

Study objectives
The use of oral TXA for 24 hours following a primary THA or TKA in addition to an intra-operative IV bolus of TXA will significantly reduce a patient's indirect blood loss at 48 hours as compared to intra-operative IV TXA in isolation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England- Cambridge East Research Ethics Committee, 10/03/2016, ref: 16/EE/0068

Study design
Phase IV single-centre open label three-arm randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Elective primary hip or knee replacement

Interventions

Current Interventions as of 28/03/2018
Randomisation of patients to Control Group 3 has stopped following the interim analysis and DMEC recommendation as outlined in section 13.4. Patients will be randomised to either Group 1 or Group 2 and treated as below.

Original Interventions:
Patients will be randomised to to Intervention Group 1, Intervention Group 2 or Control Group 3 (standard care) with an allocation ratio of 2:2:1. The trial statistician will generate the randomisation sequence. A blocked randomisation process with randomly permuted block sizes will be used.

Intervention Group 1: Tranexamic acid (1 g) will be given via IV drip during the operation plus a tranexamic acid tablet (1 g) at 2 h, 10 h, 18 h and 26 h after the operation. Patients with impaired kidney function will be given a reduced dose dependent on creatinine levels measured before the operation.

Intervention Group 2: Tranexamic acid (1 g) will be given via IV drip during the operation. Patients with impaired kidney function will be given a reduced dose dependent on creatinine levels measured before the operation.

Control Group 3: Patients receive standard care (no tranexamic acid).

For up to 48 hours, extra blood for research purposes will be taken during routine blood tests on the day of surgery and after the operation. Any adverse events will be reported. At the 90 day follow up patients will be telephoned by a research nurse and asked questions about any complications and an oxford score questionnaire will be completed. Any complications and adverse events will be reported. Belfast Orthopaedic Information System and Death registry will be checked for outpatient mortality. At the 1 year follow up patients will be seen at a routine 1 year post-surgery clinic and oxford score date will be obtained. Belfast Orthopaedic Information System and Death registry will be checked for outpatient mortality. If a patient is discharged from hospital before their 48 hour blood sample has been taken, a research nurses will visit them in their home, if consent has been given, to take the sample at the 48 hour point.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Tranexamic acid

Primary outcome(s)
Indirectly calculated blood loss (ml) 48 hours post-surgery is calculated by using red cell counts before and after surgery in a mathematical formula.

Key secondary outcome(s))
1. Incidence of post-operative haemoglobin (Hb) levels falling below the transfusion trigger (irrespective of transfusion) prior to discharge is measured from routine blood testing on day of surgery (Day 0) and post-operative Days 1-4
2. Effect of body mass index (BMI), pre-operative measure taken from the Belfast Orthopaedic

Information System (BOIS), on the volume of indirect blood loss at 48 hours (Day 2) post-operative is found using statistical analysis by the Trial Statistician
3. C-reactive protein level is measured through blood testing at baseline and 48 hours post-surgery
4. Creatinine level is measured through blood testing at baseline and 48 hours post-surgery
5. 90 day mortality is measured using the BOIS and death registry at 90 days post-surgery
6. One year mortality is measured using BOIS and death registry at 1 year post-surgery

Completion date
06/07/2020

Eligibility

Key inclusion criteria
1. Awaiting primary elective hip or knee replacement
2. Both male & female
3. Aged between 18 and 100 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
1056

Key exclusion criteria
Current participant exclusion criteria as of 28/03/2018:
1. Patients who do not pass a pre-operative assessment for elective total hip or knee arthroplasty (THA/TKA)
2. Fractured neck of femur
3. Haemophiliac or coagulation disorders that require TXA
4. Allergy to tranexamic acid or any of its excipients
5. Platelets <75,000/mm3 at pre-operative assessment*
6. Patients on active treatment for venous thromboembolism (VTE) (deep vein thrombosis (DVT), pulmonary embolisms (PE)) within 6 months of surgery*
7. History of VTE within 6 months of surgery*

8. Patients who have had a myocardial infarction (MI) within 12 months*
9. Cardiac stent within 12 months of surgery*
10. Patients who have had a stroke (cerebrovascular accident (CVA)) or transient ischemic attack (TIA) within 9 months of surgery*
11. Use of antiplatelet medication within 7 days of surgery* (Does not include aspirin if dose <300mg).Anticoagulant use within 7 days of surgery (thienopyridines, clopidogrel etc.)*
12. Direct thrombin inhibitors within 2 days of surgery*
13. Factor Xa inhibitors within 2 days of surgery*Xa inhibitors within 2 weeks of surgery*
14. The INR level is greater than or equal to 1.5 in a patient who has stopped warfarin in preparation for surgery Patients who have stopped Warfarin in preparation for surgery but have an INR level greater than or equal to 1.5*
15. Hepatic failure*
16. Patients with epilepsy
17. Patients requiring therapeutic anticoagulation post-operatively eg. metallic heart valves.
18. Pregnant women, women who have not yet reached the menopause (no menses for ≥ 12 months without an alternative medical cause) who test positive for pregnancy, are unwilling to take a pregnancy test prior to trial entry
19. Patients who have been using combined hormonal contraception (which includes combined oral contraception (COC), combined contraceptive transdermal patch and vaginal ring) within 4 weeks of surgery*.Patients who have taken the combined oral contraceptive pill within 4 weeks of surgery*
20. Female patients who are breastfeeding
21. Treated with any other investigational medication or device within 60 days
22. Patients unable to provide informed consent
23. Patients who are unable or unwilling to commit to the study schedule of events
24. Patients unwilling to provide informed consent
25. Patients who present for simultaneous bilateral THA or TKA
26. Patients who are on renal dialysis and have an AV fistula
27. Patients who previously have been enrolled in this study
*These are patients with contra-indications to primary hip or knee replacement.

Original participant exclusion criteria
1. Patients who do not pass a pre-operative assessment for elective total hip or knee arthroplasty (THA/TKA)
2. Fractured neck of femur
3. Haemophiliac or coagulation disorders that require TXA
4. Allergy to tranexamic acid or any of its excipients
5. Platelets less than 75,000/mm3at pre-operative assessment*
6. Patients on active treatment for venous thromboembolism (VTE) (deep vein thrombosis (DVT), pulmonary embolisms (PE)) within 6 months of surgery*
7. History of VTE within 6 months of surgery*
8. Patients who have had a myocardial infarction (MI) within 12 months*
9. Cardiac stent within 12 months of surgery*
10. Patients who have had a stroke (cerebrovascular accident (CVA)) or transient ischemic attack (TIA) within 9 months of surgery*
11. Anticoagulant use within 7 days of surgery (thienopyridines, clopidogrel etc.)*
12. Direct thrombin inhibitors within 2 days of surgery*
13. Xa inhibitors within 2 weeks of surgery*
14. Patients who have stopped Warfarin in preparation for surgery but have an INR level greater than or equal to 1.5*
15. Hepatic failure*
16. Patients with epilepsy

17. Patients requiring therapeutic anticoagulation post-operatively eg. metallic heart valves.
18. Pregnant women, women who have not yet reached the menopause (no menses for ≥ 12 months without an alternative medical cause) who test positive for pregnancy, are unwilling to take a pregnancy test prior to trial entry
19. Patients who have taken the combined oral contraceptive pill within 4 weeks of surgery*
20. Female patients who are breastfeeding
21. Treated with any other investigational medication or device within 60 days
22. Patients unable to provide informed consent
23. Patients who are unable or unwilling to commit to the study schedule of events

Date of first enrolment
01/07/2016

Date of final enrolment
06/07/2018

Locations

Countries of recruitment
United Kingdom

Northern Ireland

Study participating centre
Musgrave Park Hospital
Primary Joint Unit
Stockman's Lane
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Sponsor information

Organisation
The Belfast and Health Social Care Trust (BHSCT)

ROR
https://ror.org/02tdmfk69

Funder(s)

Funder type
Charity

Funder Name
Belfast Arthroplasty Research Trust (BART)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request made to Sponsor who will decide based on information provided. The point of contact for requests is Professor David Beverland, Principal Investigator (david.beverland@belfasttrust.hscni.net, +44 (0)7736679869) or Alison Murphy, Research and Development Office (ResearchSponsor@belfasttrust.hscni.net, +44 (0)28 9615 6057). Data collected as per published Protocol cannot be personally identified and will be kept by the Sponsor for five years. Informed consent was obtained from all participants and as part of this agreed to the data being used in an anonymised format in publications and at conferences. It is an ethically approved trial and the responsibility of the sponsor to ensure that all the conditions are complied with.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results for total hip arthroplasty	01/07/2021	20/01/2022	Yes	No
Results article	results for total knee arthroplasty	30/09/2021	20/01/2022	Yes	No
Protocol article	protocol	31/07/2018		Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Cost analysis	01/07/2022	10/07/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes