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Intra-articular hyaluronic acid for haemophilic ankle arthropathy

Submission date
03/09/2018

Recruitment status
No longer recruiting

Registration date
04/09/2018

Overall study status
Completed

Last Edited
09/08/2022

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
Haemophilia is the most common inherited severe bleeding disorder which puts patients at increased risk of bleeding into large joints, such as the ankle. Bleeding leads to changes within the joints, including joint lining inflammation (synovitis), and this in turn results in further bleeding and chronic (long-term) synovitis. Blood in the joint can also directly damage the cartilage, and with repeated bleeding, there is progressive destruction of both cartilage and bone. The end result is known as haemophilic arthropathy. The most common joint affected with haemophilic arthropathy is the ankle. Both the tibiotalar and the subtalar joints may be affected within the ankle. Haemophilic arthropathy affects young men and this has a significant impact on their occupation, earning capacity and participation in normal family life. Physiotherapy, painkillers and steroid joint injections are all helpful for management of haemophilic arthropathy but there is a need for a treatment for the damaged osteoarthritic joint where surgery is not appropriate. Routine options for painkillers for patients with haemophilia are limited as standard non-steroidal anti-inflammatory drugs (NSAIDs) are not allowed. COX-2 inhibitor treatment has associations in certain patient groups with increased cardiovascular (heart disease) risk. Ostenil Plus (hyaluronic acid plus mannitol) has the potential to bridge the 'treatment gap' between simple analgesia and more complex orthopaedic (surgical) solutions for haemophilic arthropathy. In particular in those patients with 'bone-on-bone' arthropathic changes, Ostenil Plus may provide cushioning to the damaged joint and in turn reduce pain and increase functionality of the joint. The potential benefits to patients may be great, and may also be more acceptable to patients when compared with an orthopaedic solution. The aim of this study is to explore whether an Ostenil Plus joint injection improves pain and functionality of the ankle joint in patients with haemophilia.

Who can participate?
Male patients aged 18 or older with haemophilia A or B and haemophilic arthropathy in one or both ankle joints

What does the study involve?
On day 1 of the study the participant completes the study questionnaires and is examined by a haemophilia doctor and a haemophilia physiotherapist. The affected joint is injected and the participant is asked to remain in the department for 30 minutes. In the following 6 months, the

participant is contacted once (at 3 months) at home (by post, email, telephone depending on their preference) and is asked to complete the study questionnaires. These should take no more than 15 minutes. A list of analgesia medication is also collected. At 6 months the participant attends again for their second injection. In the subsequent 6 months, the participant is contacted again. The number of joint bleeds is recorded during the 12 month follow-up period. This is routinely collected via a system called Haemtrack and research staff collect these data. The participant is seen for their final visit at 12 months after the first injection.

What are the possible benefits and risks of participating?
The possible benefits of this study include a reduction in pain and an improvement in mobility of an affected ankle. The risks of participating include pain at the site of injection and rarely an allergic response to the treatment. It is possible that the injection will not reduce pain or improve mobility of the affected joint.

Where is the study run from?
Churchill Hospital (UK)

When is the study starting and how long is it expected to run for?
November 2018 to August 2020

Who is funding the study?
TRB Chemedica (UK)

Who is the main contact?
Dr Nicola Curry
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
39190

Study information

Scientific Title
A single centre, open label, pilot study evaluating the effect of intra-articular hyaluronic acid injection on pain and functionality when injected into the ankle (tibio-talar and sub-talar) joint in patients with haemophilic arthropathy

Study objectives
This pilot study will explore whether Ostenil Plus joint injection improves pain and functionality of the ankle joint in persons with haemophilia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford A Research Ethics Committee, 24/10/2018, ref: 18/SC/0422

Study design
Non-randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design
Non randomised study

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
Haemophilic arthropathy of the ankle

Interventions

This study is a pilot, single centre study that will address the question: does intra-articular Ostenil Plus improve pain and functionality in participants with haemophilic arthropathy of the ankle complex. It will be run at the Oxford Haemophilia & Thrombosis Centre (OHTC), Oxford and will enrol 20 participants from either the OHTC or Basingstoke Haemophilia Centre.

A participant will be screened for eligibility using routinely collected clinical data by the staff at the Oxford Haemophilia Centre. Patients who are potentially eligible at Basingstoke hospital will be offered a patient information leaflet and will be offered an appointment to be seen in Oxford for screening. In particular an MRI scan will be reviewed to confirm the presence of haemophilic arthropathy. If the participant meets eligibility criteria, they will be invited to enter the study and sign consent.

On day 1 of the study the participant will complete the study questionnaires and will be examined by a haemophilia doctor and a haemophilia physiotherapist. Baseline clinical data will be collected. The affected joint will be injected and the participant will be asked to remain in the department for 30 minutes. The participant will have received their standard factor concentrate replacement therapy to ensure their factor blood level is adequate for the joint injection.

In the following 6 months, the participant will be contacted once (at 3 months) at home (by post, e-mail, telephone depending on their preference) and will be asked to complete the study questionnaires. These should take no more than 15 minutes and will include a pain score, HAL score, FAAM score and EQ-5D-5L. A list of analgesia medication will also be collected.

At 6 months of the study the participant will attend OHTC again for their second intra-articular injuection. They will complete the study questionnaires and will be examined by a haemophilia doctor and a haemophilia physiotherapist. The affected joint will be injected and the participant will be asked to remain in the department for 30 minutes. The participant will have received their standard factor concentrate replacement therapy to ensure their factor blood level is adequate for the joint injection.

In the subsequent 6 months, the participant will be contacted once (at 9 months) at home (by post, e-mail, telephone depending on their preference) and will be asked to complete the study questionnaires. These should take no more than 15 minutes and will include a pain score, HAL score, FAAM score and EQ-5D-5L. A list of analgesia medication will also be collected.

Numbers of joint bleeds will be recorded during the 12 month follow-up period. This is routinely collected via a system called Haemtrack and research staff will collect these data.

The participant will be seen for their final visit at the Oxford Haemophilia Centre at 12 months after the first injection. The participant will be examined by a haemophilia doctor and physiotherapist, will complete the study questionnaires and a list of analgesia medication will be collected. The factor concentrate used by the participant will be calculated for the 12 months following the first injection and compared to the 12 months prior. This assessment will involve an end of study form completion.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Hyaluronic acid, mannitol

Primary outcome measure
Pain measured by the VAS pain score; Timepoint(s): 3, 6, 9, 12 months

Secondary outcome measures
1. Functionality of the haemophilia ankle measured by the ankle HJHS score, the foot and ankle mobility measure (FAAM) and the global HJHS score at 3, 6, 9, 12 months
2. Quality of life measured by the EQ-5D-5L and Haemophilia Activity List (HAL) at 3, 6, 9, 12 months
3. Safety of treatment, including increased pain and stiffness to the injected joint at 3, 6, 9, 12 months

Overall study start date
01/11/2018

Completion date
31/08/2020

Eligibility

Key inclusion criteria
1. Written informed consent obtained before any study related activity
2. Adult male (age 18 years or older) with haemophilia A or haemophilia B of any severity, including those with inhibitors
3. MRI ankle changes consistent with haemophilic arthropathy – showing synovitic and/or degenerative changes to one or both ankle joints

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
Planned Sample Size: 20; UK Sample Size: 20

Total final enrolment
24

Key exclusion criteria

1. The patient has evidence of infection, including those patients taking antibiotic therapy
2. The patient has known inflammatory joint disease, including crystal disease
3. The patient has received an intra-articular steroid injection within the preceding 6 months
4. The patient is known to be allergic to any of the excipients of Ostenil Plus

Date of first enrolment
01/11/2018

Date of final enrolment
31/08/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Oxford Haemophilia & Thrombosis Centre
Churchill Hospital
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Sponsor information

Organisation
Oxford University Hospitals NHS Foundation Trust

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Sponsor type

Hospital/treatment centre

ROR
https://ror.org/03h2bh287

Funder(s)

Funder type
Industry

Funder Name
TRB Chemedica (UK) Ltd

Results and Publications

Publication and dissemination plan
Planned publication in a peer reviewed journal within 18 months of the study end.

Intention to publish date
28/02/2022

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		29/07/2022	01/08/2022	Yes	No
Protocol file	version 0.16	04/06/2018	09/08/2022	No	No
HRA research summary			28/06/2023	No	No