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A randomised feasibility study to assess the use of serial magnetic resonance imaging to reduce treatment times in Charcot neuroarthropathy in people with diabetes

Submission date
06/11/2017

Recruitment status
No longer recruiting

Registration date
10/11/2017

Overall study status
Completed

Last Edited
27/01/2023

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Charcot is a condition where the foot becomes hot, red and swollen, due to inflammation within the bones of the foot. This can cause fractures and dislocations within the foot. If this is allowed to continue then it can lead to foot deformity and complications such as ulcerations on the foot. The treatment for Charcot involves patients wearing a non-removable cast or walking boot, and attending regular clinic appointments. It has not known how long this treatment should last, and recommendations vary from 6 months to more than one year. Small research studies have shown that repeatedly assessing the foot with magnetic resonance imaging (MRI) could be more accurate than current methods used to monitor the condition (e.g., X-rays and measuring the temperature of the feet). MRI is a scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body. MRI may help doctors or podiatrists decide when to stop treatment, and for patients it may decrease the time that they have to wear a cast or walking boot. The current study will investigate this in more detail than previous studies have done. The aim of this feasibility study is to assess whether regularly repeating MRI scans of the foot ("serial" MRI) reduces treatment times for Charcot in people who live with diabetes.

Who can participate?
Patients aged 18 years and over with Charcot and diabetes

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive the regular magnetic resonance. Those in the second group receive the current standard assessment using repeated foot temperature measurements and regular x-rays. For participants who receive standard care this will include an MRI at the beginning of the study, and another one when the clinical team thinks the Charcot has healed. Participants in the first group receive the same standard care plus up to four additional MRI scans at 3, 6, 9 and 12 months to monitor the progression of Charcot. At the end of the study we will compare the results in the two groups. The study has two phases: the "active phase" (up to 12 months) and the "follow up phase" (6

months). Participant study involvement lasts for a maximum of 18 months. Most visits will be arranged at the same time as attendance at regular clinic visit approximately every 2 weeks during the active phase of the study. Participants may need to attend extra visits to have the additional MRI scan (s) although we will try and arrange this for the same time as the clinic visits. Participants are asked to complete a diary recording the number of times they have attended hospital, doctors or other appointments related to their health. Every three months participants are asked to complete questionnaires about how they feel and whether the Charcot is impacting on their everyday activities such as washing themselves. They are also asked to record whether the foot has been painful or not. Some participants will be invited to participate in an interview at the end of the study, to gain information into their experiences of living with Charcot and their involvement in this study. The effectiveness of treatment in preventing foot deformity will also be reported by looking at changes in plain x-rays over 18 months.

What are the possible benefits and risks of participating?
There are no direct benefits for participants taking part in the study. There will be a small increase in the amount of time participants need to spend at the hospital from 45 minutes to nearer one hour and occasionally slightly longer. There are only minimal disadvantages and risks involved in taking part in this research. Having an MRI is entirely painless. Some people find the confined space of an MRI scanner upsetting. This should not be the case in this study as only the legs and feet will need to go into the scanner. Participants will undergo a number of x-ray examinations of their foot and/or ankle. Most of these would be part of standard care, even if they do not participate in the trial, however there will be one additional x-ray examination. X-rays use ionising radiation to form images of the body and provide doctors with clinical information. The radiation dose from one of these examinations is equivalent to around four hours of natural background radiation. Exposure to radiation can cause cell damage that may after many years or decades turn cancerous. Everyone is at risk of developing cancer in their lifetime and the additional risk from the radiation exposure received in this study may be described as negligible.

Where is the study run from?
Norfolk & Norwich University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2016 to May 2021

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

Who is the main contact?
Miss Catherine Gooday (Scientific)
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Contact information

Type(s)
Scientific

Contact name
Miss Catherine Gooday

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
35344

Study information

Scientific Title
A randomised feasibility trial to define outcome measures for acute Charcot neuroarthropathy in Diabetes and their use in assessing clinical management

Acronym
CADOM

Study objectives
The aim of the study is to assess the feasibility of using serial MRI to reduce treatment times in Charcot in people with diabetes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands - Derby Research Ethics Committee, 04/10/2017, ref: 17/EM/0288

Study design
Randomised; Interventional; Design type: Diagnosis, Imaging

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 below to request a patient information sheet

Health condition(s) or problem(s) studied
Diabetes mellitus

Interventions
This study is a 2-arm open labelled randomised controlled study. It investigates the feasibility of using serial MRI to monitor CN. The study lasts for 3 years. There is an 18-month recruitment period with a further 18 month follow-up. Participants are randomly allocated to either the intervention arm or the control arm.

All participants attend for fortnightly or as per current standard care. Additional visits are arranged depending on clinical need.

In this trial a standardised assessment of serial temperature measurements are carried out. This is completed according to the trial working practice document (WPD).

To allow comparison all X-ray and MRI images are taken as per trial WPD. In both arms one X-ray is additional to usual care this is taken six months post remission. This enables the progression of foot deformity to be assessed. All participants have a baseline MRI, additional MRIs are dependent on the trial arm the participant is randomised to.

Arm A (Intervention – Standard Care and Serial MRIs)
Immobilisation discontinued on the basis of MRI defined disease resolution at three, six, nine or 12 months. In the intervention arm participants receive standard care plus additional routine MRIs at three, six, nine and 12 months. Patients randomised to serial MRI do not undergo further MRI once remission has been diagnosed i.e. if remission is diagnosed at six months the MRI at nine and 12 months will not occur.

Arm B (Control – Standard Care and one additional MRI)
Immobilisation discontinued on the basis of clinical remission determined by skin temperature measurement and MRI. Patients randomised to the usual care arm, undergo a MRI at baseline. A temperature difference of ≤ 2°C which is maintained or improves on two separate occasions for a period of ≥4weeks is the indicator to arrange the second MRI, to confirm the diagnosis of remission. If participants in either arm of the trial have not reached remission at the end of the 12 month active phase of the study they will exit the study. Ongoing usual care is provided by their clinical team.

The “active phase” – up to 12 months
These visits take place in the participant’s usual place of care (secondary care). Participants attend for fortnightly visits. Standard care and study specific procedures are carried out and recorded on the eCRF.

Once the participants in remission they move to the follow up phase of the study.

Follow up phase
Participants are transferred into a less restrictive off-loading device and then finally into footwear as per standard care. Participants continue to attend for monthly study visits for the first 3 months to monitor for any sign of relapse. Standard care will continue to be provided. The final visit occurs 6 months after remission has been diagnosed.

Intervention Type
Other

Primary outcome measure
Feasibility outcomes are assessed using eCRF reported by research teams from patient notes:
1. The proportion of patients who meet the eligibility criteria
2. The number of eligible patients recruited
3. The number of participants in which an alternative diagnosis is made during the active phase of the trial
4. The proportion of patients that withdraw or are lost to follow up
5. Statistical parameters of the key outcome measures to inform a sample size calculation for a definitive trial (estimate of effect size)
6. Ability to collect quality of life and resource use data

Secondary outcome measures
Efficacy outcome measures are assessed using the eCRF reported by research teams from patient notes:
1.1. Preliminary data on days with immobilisation at the end of the active phase of the study
1.2. Progression of foot deformity from randomisation to the end of the follow up phase of the study
1.3. Number of new ulcerations on the index foot at the end of the follow up phase of the study
1.4. Number of new ulcerations on the contralateral foot at the end of the follow up phase of the study
1.5. Number of new infections on the index foot at the end of the follow up phase of the study
1.6. Number of new infections on the contralateral foot at the end of the follow up phase of the study
1.7. Number and severity of falls (Hopkins Fall Grading System) at the end of the follow up phase of the study
1.8. Number of minor and major amputations on the index foot at the end of the follow up phase of the study
1.9. Number of minor and major amputations on the contralateral foot at the end of the follow up phase of the study
1.10. The number of participants in each arm requiring further intervention for CN (e.g. further immobilisation) within 6 months of remission

Patient Reported Outcome Measures are measured at 3, 6, 9, 12 months, at remission and at the end of the follow up phase of the study:
2.1. Level of pain is measured using the Numeric Pain Rating Scale - VAS
2.2. Health related quality of life is measured using EQ-5D-5L and SF12
2.3. Anxiety and depression is measured using the Hospital Anxiety and Depression Scale (HADS)

Economic Evaluation
3.1. Resource use is assessed through a patient diary at the end of the follow up phase of the study

Overall study start date
01/06/2016

Completion date
31/05/2021

Eligibility

Key inclusion criteria
1. Participants who are willing and have capacity to give informed consent.
2. People with diabetes as diagnosed by the WHO criteria https://www.diabetes.org.uk /Documents/Professionals/hba1c_diagnosis.1111.pdf (Appendix 1)
3. Age 18 years or over
4. New or suspected new diagnosis of acute CN (no previous incidence of acute CN within the last 6 months on the same foot) treated with off-loading
5. Understand written and verbal instructions in English

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 60; UK Sample Size: 60

Total final enrolment
43

Key exclusion criteria
1. People who have received a transplant and others receiving immunosuppressant therapy or using glucocorticoids other than in the routine management of glucocorticoid deficiency
2. Contra-indication for MRI
3. Treatment for previous suspected CN on the same foot in the last 6 months
4. Suspected or confirmed bilateral active CN at presentation
5. Active osteomyelitis at randomisation
6. Previous contralateral major amputation
7. Inability to have an MRI scan
8. Patients receiving palliative care

Date of first enrolment
01/12/2017

Date of final enrolment
30/11/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Norfolk & Norwich University Hospitals NHS Foundation Trust (Lead site)
Colney Lane
Norwich
United Kingdom
NR4 7UY

Sponsor information

Organisation
Norfolk and Norwich University Hospitals NHS Foundation Trust

Sponsor details
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/01wspv808

Funder(s)

Funder type
Government

Funder Name
NIHR Trainees Co-ordinating Centre (TCC)

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal in 2021. There are current plans to publish the study protocol.

Intention to publish date
31/12/2021

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	16/06/2020	19/06/2020	Yes	No
Other publications	Qualitative study results		29/11/2022	Yes	No
Results article		26/01/2023	27/01/2023	Yes	No
HRA research summary			28/06/2023	No	No