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A randomized controlled trial of adalimumab injection plus physiotherapy compared with placebo plus physiotherapy for patients with sciatica

Submission date
12/12/2014

Recruitment status
Stopped

Registration date
15/12/2014

Overall study status
Stopped

Last Edited
06/08/2018

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Sciatica is defined as well-localised leg pain with a sharp, shooting or burning quality that normally radiates to the foot or ankle. Current treatment in the NHS typically involves the prescribing of analgesia (painkillers) by their general practitioner, and if troublesome symptoms continue, physiotherapy. If pain persists patients are referred for more invasive treatment such as corticosteroid injection and eventually surgery. Monoclonal antibody treatments (e.g. etanercept, infliximab, adalimumab) are increasingly used to control inflammatory disease. Although expensive, they may be cost-effective if they reduce the need for more expensive treatments such as surgery. The aim of this study is to find out how effective adalimumab injections plus physiotherapy are, compared with saline (placebo) injections plus physiotherapy, for patients with sciatica whose pain is troublesome and persistent despite treatment from their GP.

Who can participate?
Adults 18 years or older with suspected sciatica who have failed primary care treatment. This will be defined as troublesome symptoms persisting for longer than four weeks, including patients whose symptoms settle but then recur, or earlier if they have severe uncontrolled pain.

What does the study involve?
At the first assessment eligibility will be checked, the study explained fully, and initial consent obtained. Participants will then be registered onto the trial. Within two to three weeks of the first assessment visit the participant will be sent for a routine blood test, tuberculosis (TB) screening including a chest X-ray, counselling by a research nurse about adalimumab; and a magnetic resonance imaging (MRI) scan to exclude any serious spinal problem. After two to three weeks participants will need to attend a second assessment at the clinic to determine if they are still eligible and confirm that counselling, TB screening, MRI and blood tests have been performed and are satisfactory. At this visit three copies of a second informed consent form will be signed and participant will begin the study. They will also complete a questionnaire asking

about their sciatica pain and how it affects their health. Participants will be randomly allocated to one of two groups. One group will receive two injections of adalimumab followed by one injection two weeks later. The other group will receive the same number of saline (placebo) injections. The injections will be prescribed by a consultant rheumatologist and administered by a rheumatology specialist nurse experienced in the administration of these injections. The first injections will be given on the same day the participant attends the second assessment at the clinic. They will also be asked which group they think they are in, and given an appointment to return two weeks later for their last injection. Both groups will also attend a course of physiotherapy which will consist of a package of treatment including exercises designed for patients with sciatica. After participants complete the physiotherapy treatment, if their symptoms have settled they will be referred back to their GP; if their symptoms persist they will be referred by their physiotherapist for further treatment in the local spinal clinic.

Follow-up questionnaires will also be sent to the participants in the post after six weeks, six and twelve months. They will contain a free post envelope for them to return. Two weeks after the twelve month questionnaire has been sent they will be contacted by a member of the research team and asked about their overall experience of the study and follow-up treatment and also asking which treatment group they thought they were in.

What are the possible benefits and risks of participating?
The possible benefits are that participants will receive physiotherapy treatment in addition to the injections, for their sciatic pain. Physiotherapy is often used for patients with sciatica and there is evidence to suggest that it helps a number of them. We hope that participants will benefit from the physiotherapy treatment. We do not know whether participants will benefit from the injections, but we hope that the information we get from the study results will help to improve the treatment options for patients with sciatica. The adalimumab used in this trial has known side-effects, but we have a great deal of experience in using it safely for illnesses like rheumatoid arthritis. The most common side-effects are reactions at the injection site, such as redness, swelling or pain. These reactions aren't usually serious. Adalimumab affects the immune system (the body's own defence system), so participants may be more likely to develop infections. At the same time, adalimumab can mask the symptoms of infection so participants may not feel as ill as they might normally do with an infection.

Where is the study run from?
The study has been set up and is being co-ordinated by the North Wales Organisation for Randomised Trials in Health and Social Care (NWORTH), and participants will be referred from primary care involving five confirmed centres (North Wales, Keele, Nottingham, London, and Cardiff) and from secondary care physiotherapy outpatient clinics.

When is the study starting and how long is it expected to run for?
It is anticipated that recruitment will start in April 2015. Participants will be enrolled on the study for a period of two years.

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK).

Who is the main contact?
Dr Nefyn Williams (nefyn.williams@bangor.ac.uk)
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Scientific

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Clinical Trials Information System (CTIS)
2015-000636-15

Protocol serial number
HTA 12/201/02

Study information

Scientific Title
A randomized controlled trial of adalimumab injection compared with placebo for patients receiving physiotherapy treatment for sciatica

Acronym
Subcutaneous Injection of Adalimumab Trial compared with Control (SCIATiC)

Study objectives
Sciatica is a symptom defined as unilateral, well-localised leg pain, with a sharp, shooting or burning quality, that approximates to the dermatomal distribution of the sciatic nerve down the posterior lateral aspect of the leg, and normally radiates to the foot or ankle.

To evaluate the effectiveness of subcutaneous injections of adalimumab plus physiotherapy compared with placebo injection of 0.9% Sodium Chloride plus physiotherapy for patients with sciatica who have failed first-line primary care treatment. Potential participants will be identified during primary care consultation, musculoskeletal service or practice database search. The primary effectiveness outcome will be sciatica-related health status using the Oswestry Disability Index. Secondary effectiveness outcomes will include pain intensity, location, duration and anticipated trajectory; the risk of poor outcome; psychological measures including fear avoidance beliefs, self-efficacy, anxiety and depression; employment status; adverse effects.

To evaluate the cost-effectiveness of subcutaneous injections of adalimumab plus physiotherapy compared with placebo injection of 0.9% Sodium Chloride plus physiotherapy for patients with sciatica who have failed first-line primary care treatment from a health service and personal social care perspective. The primary economic outcome will be the incremental cost per Quality Adjusted Life Year (QALY) gained. QALYs will be estimated by administering the EQ-5D-5L at each follow-up visit.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/1220102
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0003/144561/PRO-12-201-02.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales REC 3, 27/05/2015, REC ref: 15/WA/0105

Study design
Multi-centre randomised controlled trial and concurrent economic evaluation with internal pilot study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
All participants will be randomised to receive two doses of subcutaneous injection two weeks apart. The intervention group will receive 80 mg adalimumab followed by 40 mg in order to administer a therapeutic dose of adalimumab for a period of four weeks. The control group will

receive an equivalent volume of 0.9% Sodium Chloride. In this trial both groups will receive a concurrent course of physiotherapy intervention which can be described as 'best conservative care'. It will be delivered in local physiotherapy departments.

Intervention Type
Biological/Vaccine

Primary outcome(s)
The primary clinical outcome will be back pain specific disability using the Oswestry Disability Index measured at 12 months.
The primary economic outcomes will be the incremental cost per QALY gained, estimated by administering the EQ-5D-5L at each follow-up visit.

Key secondary outcome(s))
Other outcomes will measure: physical function, generic health status, health utility, fear avoidance beliefs, self-efficacy, anxiety & depression, employment status, use of health and personal social care services, adverse events. Secondary continuous outcome variables will be assessed in a similar way to the primary outcome variable, with the exception of time to referral for surgery, which will be assessed from trial entry using Kaplan-Meier survival analyses and the log rank test. Dichotomous variables will be explored using logistic regression. These analyses will be repeated using pre-specified participant subgroups (including the presence of neurological deficit on entry to the trial and MRI findings).
An exploratory analysis will trial the association between the clinical symptoms and MRI findings will be assessed by two independent radiologists who will interpret the proximity of the affected nerve root and the disc bulge or extrusion, and the probability that the nerve root is irritated by other pathology such as spondylosis. The level of agreement between the radiologists will be demonstrated using the kappa statistic. Clinical and MRI findings will be included in analyses of treatment response and treatment interactions.

Completion date
30/06/2018

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. 18 years of age and older
2. Clinical features of sciatica
3. Leg pain worse or as bad as back pain, obtained by asking the participant
4. Unilateral leg pain approximating a dermatomal distribution (contralateral buttock pain permitted if it does not extend below the inferior gluteal margin) obtained by asking the participant
5. One of the following:
5.1. Positive neural tension test such as straight leg raise test (SLR) restricted <50 degrees by leg pain; positive femoral stretch test
5.2. Muscle weakness or loss of tendon reflex affecting one myotome
5.3. Loss of sensation in a dermatomal distribution
6. Persistent symptoms for at least 4 weeks and less than 6 months despite first-line treatment in primary care; obtained by asking the participant

7. Moderate to high severity (≥30) on Oswestry Disability Index
8. Female partners of sexually active men should use adequate contraceptives for at least five months after the last injection. Female patients should have a negative urine pregnancy test within 2 weeks prior to randomisation, unless they are post-menopausal or have had a sterilisation operation. Sexually active men must also use adequate contraceptive methods

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Symptoms persisting for longer than 6 months obtained by asking the participant
2. A previous episode of sciatica in the last 6 months
3. Unable to perform MRI (e.g., magnetic metal implants, potential metallic intra-ocular foreign bodies, claustrophobia, extreme obesity) obtained from the medical records and by asking the participant
4. Serious spinal pathology, including cauda equina syndrome, malignancy, recent fracture, infection or very large disc prolapse which might require an urgent spinal surgery opinion, identified from participants' previous medical history in their medical records or from magnetic resonance imaging (MRI)
5. Incidental serious pathology identified by MRI (e.g., adrenal tumour)
6. Neurological deficit involving muscle weakness requiring an urgent spinal surgery assessment e.g. foot drop
7. Widespread pain throughout the body including the upper limb (pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain [cervical spine or anterior chest or thoracic spine or low back] must be present)
8. Prior use of biological agents targeting TNF-alpha within the previous 6 months obtained from the medical records and by asking participant
9. Previous lumbar spinal surgery obtained from the medical records and by asking the participant
10. Contra-indications to adalimumab injection including serious infection such as active or latent tuberculosis, transplanted organ, demyelinating disorders, malignancy, cardiac failure, low white cell count, pregnancy obtained from the medical records, results of investigations and by asking the participant
11. Pregnant or breastfeeding (women must not breastfeed for at least 5 months after the last adalimumab injection)
12. Unable to communicate in English or Welsh; unable or unwilling to give informed consent

Date of first enrolment

01/04/2015

Date of final enrolment
01/11/2016

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
North Wales Centre for Primary Care Research
Bangor University
Gwenfro Unit 4
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LL13 7YP

Study participating centre
Keele University
Arthritis Research UK Primary Care Centre
Primary Care Sciences
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Study participating centre
Sherwood Forest Hospitals NHS Trust
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Study participating centre
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Sponsor information

Organisation
Bangor University (UK)

ROR
https://ror.org/006jb1a24

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other publications	lessons learnt from discontinued trial	31/07/2018		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes