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Temporal artery biopsy vs ultrasound in diagnosis of giant cell arteritis

Submission date
18/10/2013

Recruitment status
No longer recruiting

Registration date
06/11/2013

Overall study status
Completed

Last Edited
08/06/2017

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Giant Cell Arteritis (GCA) causes inflammation and narrowing of blood vessels and can cause blindness in one third of patients. It is important that GCA is identified promptly and accurately and treated for two or more years. Currently there is no test that is 100% accurate at identifying GCA. Patients usually have new headache and scalp tenderness, typically with an abnormal blood test. However, it can be difficult to distinguish between non-serious forms of headache and GCA. Infection produces similar abnormal blood results. If there is a suspicion of GCA, treatment with steroids is started straight away. To confirm a diagnosis, a sample is taken from the blood vessel in the scalp (biopsy). This is called TAB (temporal artery biopsy). However, up to 44% of patients will show normal results in the biopsy. Therefore it is difficult to know if a patient with a normal biopsy does or does not have GCA. Stopping steroid treatment may increase the risk of blindness. Continuing treatment in a patient without GCA increases the risk of side effects. It is important to improve diagnostic tests for GCA. Another test that helps in diagnosing GCA is an ultrasound scan of the arteries on the side of the head and under the arms. Ultrasound does not involve surgery; it is a simple test which can be performed as an out-patient. In this study we aim to find out the effectiveness of the ultrasound scan.

Who can participate?
Participants with new suspicion of GCA can take part in this study.

What does the study involve?
At their first visit, all patients have initial tests like blood tests, ultrasound examination and a temporal artery biopsy (TAB) within 7 days of starting high-dose steroid treatment. Participants are treated according to usual practice and followed up as part of the study at two weeks (Visit 2) and six months (Visit 3). After six months, the accuracy of ultrasound is assessed compared with or combined with biopsy. The study also looks at whether a doctor's knowledge of the ultrasound results or the biopsy results alone, or knowledge of both results together, would affect the diagnosis and recommendation to continue or stop steroid treatment.

What are the possible benefits and risks of participating?
The potential benefit is the ability to continue or withdraw steroid treatment appropriately (rather than promptly start the treatment) on the basis of a more accurate diagnosis. If the

patient has a negative biopsy but a very positive ultrasound scan, there is the possibility that the patient would have treatment withdrawn. Participants benefit from having a non-invasive ultrasound as opposed to an invasive biopsy. This can lead to discontinuation of steroid treatment and improve quality of life. There are three possible risks. There is a possibility of delay in performing a biopsy within 7 days of starting steroid treatment. This should not be an issue as a delay in getting the ultrasound scan done is not expected. There is the possibility of withdrawing the steroid treatment in a biopsy-negative participant where the ultrasound indicates strong evidence of GCA. If the participant's doctor has ruled out GCA and is planning to withdraw steroid treatment, they must contact the trialists for the ultrasound result. It is also possible that a doctor may diagnose GCA at Visit 2 (two weeks) and continue steroid treatment, but may subsequently consider withdrawing steroids due to the possibility of an incorrect diagnosis and potential safety issues relating to steroid toxicity. In these circumstances the doctor can request the ultrasound result.

Where is the study run from?
21 hospitals across the UK (Oxford, Aylesbury, Nottingham, Westcliff-on-Sea, Romford, Portsmouth, Birmingham, Derby, Leeds, Sunderland, Dudley, Reading, Gateshead, Great Yarmouth, Harlow, Belfast), Ireland (Dublin), Norway (Kristiansand), Germany (Jena) and Portugal (Lisbon). The lead centre is the Nuffield Orthopaedic Centre, Oxford (UK).

When is study starting and how long is it expected to run for?
June 2010 to December 2014

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
Prof. Raashid Luqmani
tabul@ndorms.ox.ac.uk

Study website
http://www.ndorms.ox.ac.uk/clinicaltrials.php?trial=tabul

Contact information

Type(s)
Scientific

Contact name
Prof Raashid Luqmani

Contact details
Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science (NDORMS)
University of Oxford
Rheumatology Department
Nuffield Orthopaedic Centre
Windmill Road
Oxford
United Kingdom

OX3 7LD
+44 (0)1865 227971
raashid.luqmani@ndorms.ox.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00974883

Secondary identifying numbers
HTA 08/64/01

Study information

Scientific Title
The role of ultrasound compared to biopsy of temporal arteries in the diagnosis and treatment of Giant Cell Arteritis (GCA)

Acronym
TABUL

Study objectives
In this study the value of ultrasound examination of temporal arteries as an adjunct to diagnosis of GCA will be assessed in addition to its potential role as a substitute for temporal artery biopsy. Ultrasound examination of temporal arteries is non invasive and does not involve ionizing radiation. It can provide information about the vessel wall throughout the length of the vessel and potentially can evaluate the presence of skip lesions which are a significant problem in histological examination.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Berkshire Research Ethics Committee, 14/01/2010, ref: 09/H0505/132
TABUL Amendment 1 Approval 29/03/2011
TABUL Amendment 2 Approval 11/03/2013

Study design
Prospective cohort study using a paired design, i.e. all participants will have both ultrasound and temporal artery biopsy (TAB)

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
http://www.ndorms.ox.ac.uk/downloads/tabul-patient-info.pdf

Health condition(s) or problem(s) studied
Giant Cell Arteritis (GCA)

Interventions
All participants will have both ultrasound and temporal artery biopsy (TAB).

For the ultrasound, scans will be performed of the temporal and axillary arteries on both sides using high resolution ultrasound equipment to detect halo, stenosis or occlusion.

For the temporal artery biopsy (TAB) - a biopsy of the temporal artery from the symptomatic side.

The ultrasound scan will be carried out before the TAB and both procedures will be performed within 7 days of starting high-dose glucocorticoids. After the initial consultation at baseline (Visit 1), participants will be followed up at two weeks (Visit 2) and six months (Visit 3).

Intervention Type
Procedure/Surgery

Primary outcome measure
1. To evaluate the diagnostic accuracy (sensitivity and specificity) of ultrasound as an alternative to temporal artery biopsy for the diagnosis of GCA in patients referred for biopsy with suspected GCA (method: ultrasound scan and TAB, time point: six months)
2. To evaluate the cost-effectiveness (incremental cost per QALY) of ultrasound instead of biopsy in the diagnosis of GCA (time point: six months)

Secondary outcome measures
1. To evaluate inter-observer agreement in the assessment of ultrasound and temporal artery biopsy (time frame: six months)
2. To elicit expert views on the appropriateness of performing a biopsy following ultrasound using clinical vignettes (time frame: three years)
3. To evaluate the diagnostic accuracy (sensitivity and specificity) of the sequential diagnostic strategy from 4 as an alternative to temporal artery biopsy alone in the diagnosis of GCA (time frame: three years)
4. To evaluate the cost-effectiveness (incremental cost per QALY) of the diagnostic strategy from 4 instead of biopsy alone in the diagnosis of GCA (time frame: three years)

Overall study start date
01/01/2010

Completion date

31/12/2014

Eligibility

Key inclusion criteria
For the cohort study:
1. A clinical suspicion of new diagnosis of GCA e.g. patients with a new onset of headache, scalp tenderness, with or without elevated C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), jaw or tongue claudication with or without visual loss
2. The clinician decides that the patient requires an urgent temporal artery biopsy to determine whether or not the diagnosis is GCA
3. The patient agrees and provides consent to undergo a temporal artery biopsy as part of standard care
4. Patients have been started on high-dose glucocorticoids or will be started on high-dose glucocorticoids
5. Patients must be willing to attend for an ultrasound scan of their temporal and axillary arteries
6. Participants must be willing to give informed written consent or willing to give permission for a nominated friend or relative to provide written informed assent if they are unable to do so because of physical disabilities e.g. sudden onset of blindness/vision loss which can be caused by GCA (this will be made clear in the ethics approval application)
7. Must be 18 years of age or over

For the training cases:
1. Patients attending hospital outpatient or inpatient departments for assessment for any condition (apart from giant cell arteritis or polymyalgia rheumatica) or healthy staff volunteers
2. Above the age of 50 years
3. Willing to attend for an ultrasound scan of their temporal and axillary arteries
4. Willing and able to give written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
435-445 (in order to achieve 402 participants that have completed the primary end-point at Visit 2 [two weeks])

Key exclusion criteria
For the cohort study:
1. Previous diagnosis of GCA
2. Use of high-dose glucocorticoid (>20 mg prednisolone/day) for management of current suspected GCA for more than 7 days prior to the dates of the ultrasound and biopsy
3. Long-term (>1 month) high-dose (>20 mg per day at any time) steroids for conditions other

than polymyalgia rheumatica (PMR), within three months prior to study entry
4. Inability to give informed consent (either written consent or verbal assent from a relative or carer)
5. Inability to undergo an ultrasound scans of the temporal and axillary arteries
6. Patients with a known cause of headache (not due to GCA), or any condition which would preclude the need for a temporal artery biopsy
7. Patients who are unable to undergo an ultrasound scan and a temporal artery biopsy within 7 days of starting glucocorticoids

For the training cases:
1. Diagnosis of suspected GCA or a previous history of diagnosed or suspected GCA
2. Inability to give written informed consent
3. Inability to undergo an ultrasound scan of the temporal and axillary arteries

Date of first enrolment
01/06/2010

Date of final enrolment
01/12/2013

Locations

Countries of recruitment
England

Germany

Ireland

Norway

Portugal

United Kingdom

Study participating centre
Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science (NDORMS)
Oxford
United Kingdom
OX3 7LD

Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
Clinical Trials and Research Governance (CTRG)
Joint Research Office
Block 60
Churchill Hospital
Old Road, Headington
Oxford
England
United Kingdom
OX3 7LE
+44 (0)1865 572223
ctrg@admin.ox.ac.uk

Sponsor type
University/education

Website
http://www.admin.ox.ac.uk/researchsupport/contacts/rs/ctrg/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2016		Yes	No
Results article	results	29/03/2017		Yes	No