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Intravenous immunoglobulin (IVIg) treatment of transverse myelitis in adults and children

Submission date
08/01/2015

Recruitment status
No longer recruiting

Registration date
09/01/2015

Overall study status
Completed

Last Edited
12/12/2019

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Transverse myelitis (TM) is a rare immune-mediated disease of the spinal cord which can affect both adults and children. It causes inflammation and swelling of the spinal cord and damage to the myelin sheath surrounding the nerve cells in the spine. This stops the messages, or nerve impulses, travelling down the spinal cord from being transmitted properly. The inflammation occurs most commonly in the middle (thoracic region) of the back. Symptoms include numbness, tingling, a burning sensation and an increased sensitivity to touch, cold and heat. It also results in weakness of the arms and legs which can range from one limb feeling slightly heavy to complete paralysis. In the worse cases, sufferers can become paraplegic (paralysed from the waist down) or even tetraplegic (paralysed from the neck down); it is potentially a devastating and sometimes life-threatening condition. Patients can recover fully from TM but a large number are left significantly disabled. Neuromyelitis-optica (NMO) is an uncommon relapsing condition (a condition that keeps reappearing) where TM can be the first symptom, with damage also to the optic nerve; over time this can lead to a reduction or loss of vision. There are a number of treatments available for these conditions and evidence suggests that the sooner patients are treated, the less damage is done to the nerves and the better the long-term prognosis. The standard therapy offered is intravenous steroids over 3-5 days. However, treatment with intravenous immunoglobulins (IVIg) have also proven to be very successful as has the rather costly plasma exchange (PLEX). Ways to reduce disability in these patients are urgently required, but there is not, as present, any reliable clinical trial data that would help to determine the best form of treatment. This study looks at whether early treatment with IVIg in addition to the standard steroid therapy is of extra benefit to children and adults with TM when compared to the current standard therapy alone.

Who can participate?
Patients who are at least 1 year old and have been diagnosed with TM or NMO.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 (control group) are given the standard therapy, intravenous methylprednisolone (IV-MP), for up to 5 days. Those in group 2 (intervention group) are given the standard therapy and IVIg for up to 5 days. The patients are then followed up 6 months later to see whether there has been an improvement to

the extent and severity of damage to their spinal cord. The degree of patient disability, the extent in which this disability affects patient's lives and economic implications on the health service are also measured.

What are the possible benefits and risks of participating?
Interventions that can reduce the disability in TM patients are urgently required. The current management recommendation is largely based on expert opinion as there is no clinical trial data available to help determine the best treatment. This trial seeks to test if IVIg would be beneficial in the management of TM. As both treatments are already used in current clinical practice, participants face almost no additional risk beyond what they would experience in having the treatment.

Where is the study run from?
King's College London (UK)

When is the study starting and how long is it expected to run for?
December 2014 to November 2017

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

Who is the main contact?
Dr Onyinye Diribe

Contact information

Type(s)
Scientific

Contact name
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Clinical Trials Information System (CTIS)
2014-002335-34

ClinicalTrials.gov (NCT)
NCT02398994

Protocol serial number

17935

Study information

Scientific Title
A multicentre randomiSed controlled TRial of Intravenous immunoglobulin (IVIg) versus standard therapy for the treatment of transverse myelitis in adults and children

Acronym
STRIVE

Study objectives
Transverse myelitis (TM) is a rare immune-mediated disorder of the spinal cord affecting children and adults, characterised by a rapid onset of paraplegia or tetraplegia, loss of sensation and sphincter disturbance; in severe cases, it is potentially a devastating and sometimes life threatening condition. There are various treatments for these conditions and evidence suggests that the sooner they are administered, the less damage that is done to the nerves and the better the long term prognosis. At present the standard therapy that is offered is intravenous steroids for 3-5 days, although treatment with intravenous immunoglobulins (IVIg) has also proven to be very successful, as has plasma exchange (PLEX), although the latter is very costly. Strategies to reduce disability in these patients are urgently required, yet there are no robust controlled trials to inform on optimal treatment. This will be a multicentre, randomised controlled trial involving children and adults, to evaluate if the early addition of IVIg treatment to standard therapy with intravenous steroids is of extra benefit in TM, when compared to the current standard therapy alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central - Berkshire B, 30/10/2014, ref: 14/SC/1329

Study design
Randomised; Interventional

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Children, Neurological disorders; Subtopic: All Diagnoses, Neurological (all Subtopics); Disease: Nervous system disorders, All Diseases

Interventions
Admin of immunoglobulin, Eligible participants will be randomised to treatment or control group.
1. Participants randomised to the control arm of this study will be prescribed intravenous methylprednisolone in line with the local clinical practice (variations of practice will be recorded)

2. Paediatric patients (treatment arm) will receive 30mg/kg or 500 mg/m2 capped to a maximum dose of 1g/day for 5 days
3. Adult patients (treatment arm) will be given 1gram/day for 5 days

Intervention Type
Drug

Phase
Not Applicable

Primary outcome(s)
Improvement of 2 points or greater on the ASIA Impairment scale (classfiied A-E); Timepoint(s): 6 months

Key secondary outcome(s))
1. Change in ASIA motor scale (0-100) and ASIA sensory scale (0-112) at 3, 6, and 12 months post randomisation
2. Change in Kurtzke expanded disability status scale (EDSS) measured by Neurostatus scoring at 3, 6, and 12 months
3. EQ-5D-Y for patients aged 8-12 years (at presentation) at 3,6 and 12 months post randomisation
4. EQ-5D-5L for patients aged ≥ 13 years (at presentation) at 3, 6 and 12 months post randomisation
5. Individuals ≥ 13 years at presentation: International SCI Quality of Life Basic Data Set at 3, 6 and 12 months post randomisation
6. Client Service Receipt Inventory (CSRI) at 3, 6 and 12 months post randomisation

Completion date
11/05/2016

Eligibility

Key inclusion criteria
Patients will be eligible for inclusion on the trial if on presentation they:
1. Are aged 1 year or over
2. Have been diagnosed with:
2.1. EITHER acute first onset transverse myelitis
(The TM CONSORTIUM WORKING GROUP 2002 criteria for probable TM will be used. Hence, following clinical and radiological exclusion of a compressive myelopathy, patient will be diagnosed to have TM if they meet all the following criteria:
2.1.1. Sensory, motor, or autonomic dysfunction attributable to the spinal cord
2.1.2. Bilateral signs and/or symptoms (not necessarily symmetric)
2.1.3. Sensory level (except in young children <5 years where this is difficult to evaluate)
2.1.4. Lack of MRI brain criteria consistent with MS (McDonald 2010 space criteria)
2.1.5. Progression to nadir between 4 h and 21 days)
2.2. OR Have been diagnosed with first presentation of neuromyelitis optica.
(Patients with definite modified NMO will meet the following criteria (Wingerchuck et al, 2006).
Absolute criteria, both:
2.2.1. Optic neuritis
2.2.2. Acute myelitis
2.3. Plus two out of three supportive criteria:

2.3.1. Brain MRI not meeting criteria for MS at disease onset
2.3.2. Spinal cord MRI with contiguous T2weighted signal abnormality extending over three or more vertebral segments, indicating a relatively large lesion in the spinal cord
2.3.3. AQP 4 seropositive status)
3. Have an ASIA Impairment score of A, B or C
4. Have commenced steroid treatment but will be randomised no later than day 5 of steroids, and if definitely known, randomisation will not exceed 21 days from the onset of symptoms
5. Give assent (8-16 years)/consent to participate in the trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Sex
All

Key exclusion criteria
Patients would be excluded if they show evidence of:
1. Contraindication to IVIg as stated in the product SmPC, or receiving IVIG for other reasons
2. Previously known systemic autoimmune disease (eg systemic lupus erythematosus) or any evidence of systemic inflammation during current presentation.
3. Direct infectious aetiology (eg varicella zoster)
4. Previous episode of CNS inflammatory demyelination
5. Acute disseminated encephalomyelitis (ADEM)
6. Other causes of myelopathy not thought to be due to myelitis (eg nutritional, ischaemic, tumour etc.)
7. Other disease which would interfere with assessment of outcome measures
8. Pregnancy
9. Circumstances which would prevent follow-up for 12 months

Date of first enrolment
04/03/2015

Date of final enrolment
11/03/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

King's College London
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Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2017		Yes	No
Protocol article	protocol	25/05/2015		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes