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Cluster randomised trial of an intervention to promote implementation of clinical guidance on the management of suspected encephalitis

Submission date
22/07/2013

Recruitment status
No longer recruiting

Registration date
22/07/2013

Overall study status
Completed

Last Edited
11/12/2018

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Up to twenty eight hospitals will be recruited across the UK to take part in this study which will evaluate the effects of an intervention to improve the clinical management of patients with suspected encephalitis (inflammation of the brain) in secondary care. This will involve assessing adherence to the national guidelines for encephalitis and developing and applying an intervention to improve adherence. The development of the intervention will be informed by existing evidence on professional behaviour change and sub-studies within the ENCEPH UK programme. The intervention will target clinicians responsible for the diagnosis and initial management of suspected encephalitis. Cost effectiveness and clinical outcomes will be assessed. The study aims to give clinicians evidence-based tools to help them implement the national guidance for management of suspected encephalitis patients.

Who can participate?
Any patients in whom encephalitis should have been suspected within the recruited sites will be included in the study.

What does the study involve?
Hospitals will be randomly allocated to either the standard care group or the intervention group. The intervention will target clinicians responsible for the diagnosis and initial management of suspected encephalitis. Nurses will collect data from the patients' notes and this will be recorded on the data collection forms in a similar style to a clinical audit. No identifiable data such as name or NHS number will be recorded; the patients' date of birth and gender will be collected so that we can categorise the population. The hospital will keep the key of which patient has been allocated to each number so that data queries can be checked; however, this encryption key will remain at the hospital.

What are the possible benefits and risks of participating?
Ideally, all hospitals should be following accepted best practice in the care of suspected

encephalitis. However, we know this is not the case. Should the intervention be effective, patient care in intervention hospitals should improve. We do not foresee any additional risks to patients in either group of the study.

Where is the study run from?
This study is being run by Brain Infections UK within The University of Liverpool. Up to 28 hospitals will be recruited across the UK.

When is the study starting and how long is it expected to run for?
This study is due to start data collection in January 2014 and will run for a further 2 years.

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

Who is the main contact?
Prof Tom Solomon, Chief Investigator
Dr Ruth Backman, Trial Coordinator, R.Backman@liverpool.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Ruth Backman

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
14688

Study information

Scientific Title
Development and evaluation of an intervention based around the national guidelines on the management of suspected encephalitis, and its evaluation through a cost-effectiveness analysis

Acronym
ENCEPH UK Intervention RCT

Study objectives
Up to 28 hospitals will be recruited across the UK to take part in this cluster randomised controlled trial which will evaluate the effects of an intervention to improve the clinical management of suspected encephalitis in secondary care. The cost effectiveness of the intervention will also be assessed. The study will be run over two years including a 12-month follow-up intervention period.

Within this study we will compare the rate of diagnosis for encephalitis between the 'routine' hospitals and intervention hospitals. The development of the intervention will be informed by existing evidence on professional behaviour change and sub-studies within the ENCEPH UK programme. The intervention will target clinicians responsible for the diagnosis and initial management of suspected encephalitis. The use of a cluster randomised controlled trial in up to twenty eight hospitals with a follow-up period of 12 months will allow both cost effectiveness and clinical outcomes to be assessed.

The main outcome will be the proportion of patients with suspected encephalitis appropriately investigated and started on treatment with aciclovir within 6 hours and those patients that had a lumbar puncture performed within 12 hours (unless it was clinically contraindicated).

Added 07/01/2015:
We will explore the outcome data to examine any relationship between the method of inclusion and compliance of the primary outcomes and if there is a difference in case mix, our modelled primary outcome analysis will adjust for this.

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=14688

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES committee North West - Preston, 03/05/2013, ref:13/NW/0279

Study design
Cluster randomised controlled interventional trial

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
For this study we will not be actively recruiting patients as it is a retrospective notes review which is in a similar style to a robust clinical audit. Therefore there are no patient information sheets associated with this project.

Health condition(s) or problem(s) studied
Topic: Infection; Subtopic: Infection (all Subtopics); Disease: Infectious diseases and microbiology

Interventions
Package 1, there will be a series of interventions within the package that will be clinical led to help implement the national guidelines for management of suspected encephalitis patients.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Current primary outcome measures as of 07/01/2015:
The proportion of patients with suspected encephalitis whose care met all of the following criteria:
1. Aciclovir given within 6 hours of admission to hospital
2. A LP was performed within 12 hours of hospital arrival unless clinically contraindicated

Previous primary outcome measures:
The proportion of patients with suspected encephalitis whose care met all of the following criteria:
1. Aciclovir given within 6 hours of admission to hospital at the appropriate dose unless there was an alternative diagnosis
2. A LP was performed within 12 hours of hospital arrival unless clinically contraindicated.

Secondary outcome measures
Current secondary outcome measures as of 07/01/2015:
1. The proportion of all adults started on intravenous (IV) aciclovir within an appropriate dosage range for a neurological presentation who met the definition of suspected encephalitis
2. The proportion of all children started on intravenous (IV) aciclovir within an appropriate dosage range for a neurological presentation who met the definition of suspected encephalitis
3. The proportion of patients with suspected encephalitis who had a lumbar puncture performed within 12 hours unless there was a clinical contraindication
4. The proportion of patients with suspected encephalitis who had a lumbar puncture at any time within the index presentation
5. The proportion of patients with suspected encephalitis who had either MRI or CT scan within 24 hours of admission
6. The proportion of patients with suspected encephalitis having had a lumbar puncture, who had the following CSF investigations performed:
6.1. CSF:serum glucose ratio calculated
6.2. HSV PCR performed

7. An evaluation of the primary outcomes comparing adults and children enrolled in the RCT
8. A cost-effectiveness evaluation of the intervention

Previous secondary outcome measures:
1. The proportion of all adults given intravenous (IV) aciclovir for a neurological presentation who met the definition of suspected encephalitis.
2. The proportion of all children given IV aciclovir for a neurological presentation who met the definition of suspected encephalitis.
3. The proportion of patients with suspected encephalitis who had a lumbar puncture performed within 12 hours unless there was a clinical contraindication.
4. The proportion of patients with suspected encephalitis who had a lumbar puncture after resolution of a clinical contraindication to that LP.
5. The proportion of patients with suspected encephalitis who had either MRI or CT scan within 24 hours of admission.
6. For patients with HSV encephalitis, the proportion who die, have sequelae and appear to make a full recovery upon discharge.
7. The proportion of patients with suspected encephalitis having had a lumbar puncture, who had the following CSF investigations performed:
7.1. CSF:serum glucose ratio calculated
7.2. HSV PCR performed
8. An evaluation of the primary outcomes comparing adults and children enrolled in the RCT.
9. A cost-effectiveness evaluation of the intervention.

Overall study start date
20/01/2014

Completion date
15/07/2016

Eligibility

Key inclusion criteria
Site inclusion criteria:
All centres will have a consultant and all centres must be equipped with the ability to perform, or have access to CT/MRI scans and have aseptic conditions for conducting a LP to be performed. Hospitals will be randomised as a unit to either the standard care or intervention arm. Study centres will be initiated once all global (e.g. local research and development [R&D] approval) and study-specific conditions (e.g. training requirements) have been met, and all necessary documents have been returned to the Brain Infections UK coordinating centre.
Within this study, any patients who have suspected encephalitis within the recruited sites will be included in the study. The inclusion criteria for suspected encephalitis are:

Patients with suspected encephalitis
(a) Mandatory
Acute or sub-acute (<4 weeks) alteration in consciousness, cognition, personality or behaviour persisting for more than 24 hours. Personality/behaviour change includes: agitation, psychosis, somnolence, insomnia, catatonia, mood liability, altered sleep pattern and (in children): new onset enuresis, or irritability.
Plus ANY two of:
1. Fever (> 38°C) / prodromal illness acute or sub-acute
2. Seizures: new onset

3. Focal neurological signs acute or sub-acute onset. These include:
3.1. Focal weakness
3.2. Oromotor dysfunction
3.3. Movement disorders (chorea, athetosis, dystonia, hemiballisms, stereotypies, orolingual dyskinesia and tics) including Parkinsonism (bradykinesia, tremor, rigidity and postural instability)
3.4. Amnesia
4. Pleocytosis: cerebrospinal fluid white cell count >4 cells/ul
5. Neuroimaging: compatible with encephalitis
6. Electroencephalogram (EEG): compatible with encephalitis
OR
(b) Clinical suspicion of encephalitis but above investigations have not yet been completed
OR
(c) Clinical suspicion of encephalitis and the patient died before investigations completed

Target Gender: Male & Female

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: Up to 1680; UK Sample Size: 1120 Up to 1680

Key exclusion criteria
Site exclusion criteria:
Current participation in the ENCEPH UK programme

Added 07/01/2015:
Patient exclusion criteria
Any patient aged under 28 days upon the date of admission shall be excluded

Date of first enrolment
03/02/2014

Date of final enrolment
31/05/2015

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
Blackpool Victoria Hospital
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Queen Elizabeth Hospital
Gateshead
United Kingdom
NE9 6SX

Study participating centre
Queen Alexandra Hospital
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Doncaster Royal Infirmary
Doncaster
United Kingdom
DN2 5LT

Study participating centre
Stepping Hill Hospital
Stockport
United Kingdom
SK2 7JE

Study participating centre
Whiston Hospital
Prescot
United Kingdom
L35 5DR

Study participating centre

University Hospital Coventry and Warwick
Coventry
United Kingdom
CV2 2DX

Study participating centre
Addenbrooke's Hospital
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Countess of Chester Hospital
Chester
United Kingdom
CH2 1UL

Study participating centre
North Devon District Hospital
Devon
United Kingdom
EX31 4JB

Study participating centre
North Tees Hospital
Stockton-on-Tees
United Kingdom
TS19 8PE

Study participating centre
Bedford Hospital
Bedford
United Kingdom
MK42 9DJ

Study participating centre

Gloucestershire Royal Hospital
Gloucester
United Kingdom
GL1 3NN

Study participating centre
King's Mill Hospital
Sutton-in-Ashfield
United Kingdom
NG17 4JL

Study participating centre
Royal Sussex County Hospital
Brighton
United Kingdom
BN2 5BE

Study participating centre
Ormskirk and Southport Hospital
Ormskirk
United Kingdom
L39 2AZ

Study participating centre
West Suffolk Hospital
Bury St Edmunds
United Kingdom
IP33 2QZ

Study participating centre
Leicester Royal Infirmary
Leicester
United Kingdom
LE1 5WW

Study participating centre

Russells Hall Hospital
Dudley
United Kingdom
DY1 2HQ

Study participating centre
Luton and Dunstable Hospital
Bedford
United Kingdom
LU4 0DZ

Study participating centre
Great Western Hospital
Swindon
United Kingdom
SN3 6BB

Study participating centre
Ysbyty Gwynedd
Gwynedd
United Kingdom
LL57 2PW

Study participating centre
East Surrey Hospital
Redhill
United Kingdom
RH1 5RH

Study participating centre
Chesterfield Royal Hospital
Chesterfield
United Kingdom
S44 5BL

Sponsor information

Organisation
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Sponsor details
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Sponsor type
University/education

Website
http://www.liv.ac.uk/

ROR
https://ror.org/04xs57h96

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

Publication and dissemination plan

The protocol is published and can be found at http://www.implementationscience.com/content/10/1/14. The paper describing the formation of the intervention package has been editorially accepted and we will publish the final trial results and a process evaluation at the end of data collection.

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	27/01/2015		Yes	No
Results article	results	01/12/2015		Yes	No
Results article	results	06/12/2018		Yes	No
HRA research summary			28/06/2023	No	No