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Antibiotics to Prevent Infections in Stroke

Submission date 25/07/2007	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 05/09/2007	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 11/09/2018	**Condition category** Circulatory System	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Nearly 40% of patients with acute stroke (one that has happened within the last few hours) find it difficult to swallow. If a person is not able to swallow properly, there is a risk that food or drink may get into the windpipe and, ultimately, the lungs. This can lead to chest infections. Despite measures such as positioning the patient in the bed and changing the consistency of foods to make them easier to swallow, one in five stroke patients will develop chest infections. These chest infections lead to the increased possibility of deaths and disability following a stroke. A possible solution to this might be to give stroke patients with difficulty swallowing antibiotics for the first 7 days to try and prevent chest infections while waiting for their swallowing to improve. However, this has yet to be tested and it is possible that it may lead to clostridium difficile diarrhoea, development of antibiotic resistance or other adverse effects of antibiotics. In short, it is currently unclear as to whether the potential benefits of preventive antibiotics outweigh the possible risks. The aim of this study, therefore, is to find out the benefits and safety of an "act first" approach, where antibiotics are given for 1 week to patients with swallowing problems, compared with a "wait and watch" approach in preventing chest infections or deaths after a stroke.

Who can participate?
Patients who have had a stroke within the last 48 hours and have been assessed as being unable to swallow.

What does the study involve?
Fifty stroke units are randomly allocated to one of two groups. The 'act first' group will prescribe preventive antibiotics to stroke patients that are unable to swallow. The 'wait and watch' group are monitored for chest infections but not given preventive antibiotics.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Kings College Hospital NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
July 2008 to August 2014

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

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
KCH-STR-INF v1.2

Study information

Scientific Title
A cluster randomised trial of different strategies of antibiotic use to reduce the incidence and consequences of chest infection in acute stroke patients with swallowing problems

Acronym
STROKE-INF

Study objectives
The main hypothesis for the study is that prophylactic use of antibiotics (an "act first" approach) in acute stroke patients with swallowing problems on a bedside clinical assessment will be better than the current practice of monitoring for infection and treatment if necessary (a "wait and watch" approach) in reducing chest infections and their consequences in stroke patients.

On 12/11/2008 the overall trial start date was changed from 01/04/2008 to 29/04/2008.

On 30/06/2014 the following changes were made to the trial record:
1. At the time of amendment, the public title was changed from "A cluster randomised trial of

different strategies of antibiotic use to reduce the incidence and consequences of chest infection in acute stroke patients with swallowing problems" to "Antibiotics to Prevent Infections in Stroke".
2. The following scientific title was added "A cluster randomised trial of different strategies of antibiotic use to reduce the incidence and consequences of chest infection in acute stroke patients with swallowing problems" and also the following acronym, "STROKE-INF Study".
3. The overall trial end date was changed from 31/03/2010 to 31/08/2014.
4. The target number of participants was changed from 800 to 1200.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wandsworth Research Ethics Committee, South London REC Office (1), 26/02/2008, REC ref: 08/H0803/1

Study design
Pragmatic cluster randomised controlled trial with blinded follow-up

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Stroke/acute care/complications

Interventions
All patients will be managed in stroke unit settings and receive supportive care for dysphagia patients as recommended by the Royal College of Physicians Stroke Guidelines. The intervention being investigated is an "act first" strategy of prophylactic antibiotic use versus a "wait and watch" strategy of monitoring and treating only if signs of infection develop. Pathogens involved in aspiration pneumonia include gram negative bacilli (40 - 60%) and gram positive cocci (20 - 40%), with anaerobes being rare.

Treatment of aspiration pneumonia is currently empirical, and the British Thoracic Society recommends a combination of a cephalosporin with a macrolide as initial treatment. However, cephaolosporins are associated with a high incidence of C difficile infections, the reduction of which is a high priority NHS target. Many hospital guidelines prefer the use of amoxycillin as the first line antibiotic, hence we will use amoxicillin (with or without clavulanate potassium) as the antibiotic of preference.

In the "act first" group, prophylactic treatment with amoxicillin (or equivalent co-amoxyclav) and clarithromycin will be given for 7 days via a Nasogastric (NG) tube or intravenously if the patient has no NG access. Patients in the "wait and watch" group will be monitored for chest infections and empirical treatment will be commenced with antibiotics recommended as recommended by hospital infection policy or indicated by microbiological tests.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Coamoxyclav, clarithromycin

Primary outcome(s)
The clinical primary outcome measure is the incidence of chest infections in the first 14 days after stroke onset. This will be defined as a temperature greater than 37.5°C on two consecutive measurements or a single measurement of greater than 38.0°C with chest symptoms and one or more of the following:
1. White cell count greater than 11,000/mL
2. Pulmonary infiltrate on chest x-rays
3. Positive microbiology cultures

The primary cost outcome measure will be the total hospital costs (acute and rehabilitation) for the initial episode of care, calculated as a product of costs per day for type of care (standardised NHS tariff) and number of days spent in each care setting.

Key secondary outcome(s))
Current secondary outcome measures as of 30/06/2014:
1. C. difficile diarrhoea, concordance with protocol treatment, discontinuation of prophylaxis or use of additional antibiotics
2. New onset of MRSA infection
3. Adverse Event (AE), Adverse Reaction (AR), Serious Adverse Event / Reaction (SAE / SAR), and Suspected Unexpected Serious Adverse Reactions (SUSAR) as defined per protocol. (Protocol KCH-STR-INF v7.0, 27th July 2011 (2007-004298-24)
4. Death, or chest infection at 14 days of stroke onset
5. National Institute of Health Stroke Scale (NIHSS) at 14 days of stroke onset or at discharge if sooner
6. Change in NIHSS from baseline at 14 days of stroke onset or at discharge if sooner
7. Modified Rankin Scale at 90 (± 14) days post-stroke
8. Patients achieving dichotomised modified Rankin Scale score (mRS 0-2) at 90 (± 14) days post-stroke
9. Ordinal regression analysis of mRS at 90 (± 14) days post stroke
10. Mortality, institutionalisation and mortality or institutionalisation at 90 (± 14) days post stroke
11. EuroqUROQOL EQ-5D-3L and EQ-VAS -5D VAS scores as a whole and comparisons of the domains in the scale at 90 (± 14) days post stroke.
12. Discontinuation of antibiotic prophylaxis in the intervention group (< 4 days of treatment)
13. Antibiotic use in the control group within 7 days of stroke onset
14. Duration of hospital stay
15. Participation in programmed assessment or therapy activities, measured as the number and duration of supervised rehabilitation during hospital stay.
16. Incremental cost-effectiveness ratios (ICERs) if either the intervention or control approach involves an additional cost alongside an improvement in outcome (ICERs will then represent the cost per 1% reduction in incidence of chest infection and/or cost per quality-adjusted life-year (QALY) gained).

Previous secondary outcome measures:
1. Adverse events related to antibiotic use including:

1.1. Antibiotic related side-effects
1.2. New onset of Methicillin Resistant Staphylococcus Aureus (MRSA) infection
1.3. C. difficile diarrhoea
2. Mortality, institutionalisation and measures of activity (Functional Independence Measure), participation (Rankin Scale), mood (Hospital Anxiety and Depression Scale) and quality of life (Euroqol 5D and Visual Analogue Scale [VAS]) at three months
3. Total duration of hospital stay

Secondary economic outcome measures will include Incremental Cost-Effectiveness Ratios (ICERs) and Quality-Adjusted Life-Years (QALY) gained by the intervention.

Completion date
31/08/2014

Eligibility

Key inclusion criteria
The study will be undertaken in hospital based stroke units that have a defined policy for acute stroke care and participate in the National Stroke Audit (NSA). It will include:
1. Ischaemic or haemorrhagic stroke patients within 48 hours of symptom onset
2. Unable to swallow because of impaired consciousness levels or have failed the clinical bedside swallowing assessment performed by a trained professional

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Not Specified

Sex
All

Key exclusion criteria
1. Pre-existing swallowing problems
2. Evidence of infection or pyrexia at the time of admission
3. Allergy to penicillins or macrolides
4. Antibiotic treatment within the week prior to inclusion
5. Lack of consent from the patient or next of kin

Date of first enrolment
01/07/2008

Date of final enrolment
31/08/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College London
London
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SE5 9PJ

Sponsor information

Organisation
King's College Hospital NHS Foundation Trust (UK)

ROR
https://ror.org/01n0k5m85

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (UK) (ref: PB-PG-0906-11103)

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	07/11/2015		Yes	No
Results article	results	01/02/2019		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes