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Metoclopramide and selective oral decontamination for avoiding pneumonia after stroke

Submission date 29/09/2016	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol
Registration date 10/10/2016	**Overall study status** Stopped	[_] Statistical analysis plan [_] Results
Last Edited 05/04/2019	**Condition category** Circulatory System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

A stroke is a serious, life-threatening medical condition that occurs when the blood supply to part of the brain is cut off. People who have had a stroke often lose the ability to swallow. This can cause food and saliva to get into their airways. If this happens, there is an increased risk of developing pneumonia, which is a life threatening and highly weakening condition. Even treatment with antibiotics may not prevent the weakening effects of pneumonia from delaying recovery, or worsening the condition. In such stroke patients, food is provided through a tube directly into the stomach to prevent food entering the airways. Stroke patients are still at risk however, as moving and turning can lead to vomiting. Vomit can easily be inhaled into airways, especially when lying down. Additionally saliva, containing bacteria that can cause pneumonia when inhaled, can build up as the patient cannot swallow. The aim of this study is to test two ways of preventing pneumonia in stroke patients who are being fed through a tube. The first method is to prevent patients vomiting using a drug called metoclopramide. This drug is well known to prevent vomiting and the NHS use it widely in other patients. The second method is to use an antibiotic paste in the patient's mouth to reduce the bacteria in their saliva. Both methods have been shown in smaller studies to decrease the number of patients who develop pneumonia and the number of resulting deaths.

Who can participate?

Adult patients who have had a stroke within the last 9 hours, who have swallowing problems and are receiving tube feeding

What does the study involve?

All participants receive a 'drug' and a 'mouth paste' but neither the participant nor the clinicians know whether the participant is getting a 'real' drug or paste or a placebo (dummy). Participants are randomly allocated into four groups:

1. Metoclopramide and placebo paste
2. Metoclopramide and antibiotic paste
3. Placebo metoclopramide and antibiotic paste
4. Placebo metoclopramide and placebo paste

Participants are monitored daily for signs and symptoms of pneumonia, as well as any treatment side effects for 14 days. On day 30, participants are assessed to see how they are recovering from their stroke. On day 90, participants and/or their families receive a phone call from the study team to see how they are doing, how they are eating (is the tube still in), where they are living (home, care home, hospital) and assess their quality of life. All collected data is analysed by the team to see if either treatment can prevent pneumonia and reduce the number of deaths in these patients, and to see if there are cost savings from preventing pneumonia by reducing length of stay, accelerating rehabilitation and preventing use of systemic antibiotics. Antibiotic resistance is a growing problem and reduction in antibiotic use is an important national target for the NHS.

What are the possible benefits and risks of participating?
The participant may be given metoclopramide for a longer period than for up to 21 days. Metoclopramide is normally given for 5 days to prevent vomiting although it can be given for longer. The main side effect of this is tardive dyskinesia (involuntary movements of the face and jaw), although this tends to develop well after the 21 days this study is proposing it be used for. The patient will be observed on a daily basis and if these symptoms start to occur, the use of the drug will be stopped. The mouth paste is currently not licenced for use in the UK, although it is widely used in the Netherlands. As with all antibiotic treatment it has the potential to cause antibiotic resistance and patients will be monitored for this.

Where is the study run from?
Fifty different hospitals from across the UK, led by Keele University (UK)

When is the study starting and how long is it expected to run for?
January 2017 to September 2019

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

Who is the main contact?
Prof. Christine Roffe

Study website
www.keele.ac.uk/maps2

Contact information

Type(s)
Scientific

Contact name
Prof Christine Roffe

ORCID ID
http://orcid.org/0000-0002-5259-6649

Contact details
Institute for Applied Clinical Sciences (IACS)
Keele University
Guy Hilton Research Centre

Thornburrow Drive
Hartshill
Stoke-on-Trent
United Kingdom
ST4 7QB

Additional identifiers

EudraCT/CTIS number
2016-003406-14

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 14/49/154

Study information

Scientific Title
The Metoclopramide and selective oral decontamination for Avoiding Pneumonia after Stroke (MAPS-2) Trial: a 2x2 double-blind, randomised controlled trial of metoclopramide and selective oral decontamination for the prevention of pneumonia in patients with dysphagia after an acute stroke

Acronym
MAPS-2

Study objectives
Early interventions aimed at the prevention of pneumonia reduce mortality and improve recovery after stroke.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/1449154

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West-Greater Manchester Central Research Ethics Committee, 04/04/2017, ref: 17/NW /0058

Study design
2x2 factorial double-blind randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files.

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

Interventions
This study will test two ways of preventing pneumonia in stroke patients who are being fed through a tube. The first method will be to prevent patients from vomiting using a drug called metoclopramide. This drug is well known to prevent vomiting and the NHS use it widely in other patients. The second method is to use an antibiotic paste in the patient’s mouth to reduce the bacteria in their saliva. Both methods have been shown, in smaller separate studies, to decrease the number of patients who develop pneumonia and the number of resulting deaths. All patients recruited will receive a 'drug' and a 'mouth paste' but neither the patient nor the clinicians will know whether the patient is getting a 'real' drug or paste or a placebo. Patients are randomised into four groups:
1. Metoclopramide and placebo paste
2. Metoclopramide and antibiotic paste
3. Placebo metoclopramide and antibiotic paste
4. Placebo metoclopramide and placebo paste

Patients will then be monitored daily for signs and symptoms of pneumonia, as well as any treatment side effects for 14 days (as of 04/09/2017 this has been updated to 21 days). On day 30, patients will be assessed to see how they are recovering from their stroke (neurologically). On day 90, patients and/or their families will receive a phone call from the MAPS-2 team to see how they are doing physically, how they are eating (is the tube still in), where they are living (home, care home, hospital) and what quality of life is like for them. All collected data will be analysed by the team to see if either treatment can prevent pneumonia and reduce the number of deaths in these patients. Health economics will be analysed to see if cost savings result from preventing pneumonia by reducing length of stay, accelerating rehabilitation and preventing use of systemic antibiotics.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Metoclopramide, SOD Paste is made up of colistin, tobramycin and amphotercin b

Primary outcome measure
Mortality up to the end of the study (90 days). The patients' vital status will be assessed during months 26-32, giving a maximum follow-up of 24 months for participants recruited in month 1

and 3 months for participants recruited at the end of the study. This will be done by phone call to the GP, and, where necessary, the participant or the contacts they provide. Missing data will be ascertained with the team who recruited the patient, and via linkage with Hospital Episode Statistics, Office of National Statistics, and Sentinel Stroke National Audit datasets.

Secondary outcome measures
1. Pneumonia within 14 days. This is taken from data collected on the daily log. The study team will look at the clinical diagnosis and indication for antibiotics and CDC and modified MANN criteria.
2. Number of days of antibiotic treatment for pneumonia within the first 30 days
3. Neurological recovery measured using the National Institutes of Health Stroke Scale (NIHSS) at 30 days
4. Disability measured using the modified Rankin Scale (mRS) at 90 days
5. Quality of life measured using the EuroQol five dimensions questionnaire (EQ-5D) at 90 days

Overall study start date
01/01/2017

Completion date
01/10/2020

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Adult patients with a clinical diagnosis of acute stroke
2. Within 9 hours of stroke onset
3. Moderate to severe neurological impairment with and NIHSS score of 10 or above
4. Unable to take a normal oral diet or fluids because too drowsy to be assessed formally or failed bedside assessment of swallowing

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
1160

Key exclusion criteria
1. Evidence of vomiting since stroke onset
2. Pre-existing swallowing problem
3. Known oesphageal pathology that might interfere with placement of a nasogastric tube
4. Probable or definite pneumonia

5. Contraindications to metroclopramide, epilepsy, gastrointestinal obstruction, perforation, or haemorrhage, gastrointestinal surgery within the last week, Parkinson's disease, treatment with levodopa or dopaminergic agonists, phaeochromocytoma or neuroleptic maligant syndrome or tardive dyskinesia or methaemoglobinaemia or NADH cytochrome
6. Patients with severe liver disease or kidney disease
7. Known allergy to colistin
8. Pregnant or breastfeeding
9. Other co-morbid conditions with a life expectancy of less than 3 months at the discretion of the clinical treating team
10. Inability to gain consent from the patient or a legal representative or refusal of consent

Date of first enrolment
01/12/2017

Date of final enrolment
31/03/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Stroke Research Group
Institute of Applied Clinical Sciences
Keele University
Guy Hilton Research Centre
Thornburrow Drive
Hartshill
Stoke-on-Trent
United Kingdom
ST4 7QB

Sponsor information

Organisation
University Hospitals North Midlands (UHNM) NHS Trust

Sponsor details
R&D Department
Courtyard Annexe
Royal Stoke Hospital-UHNM
Newcastle Road
Stoke-on-Trent

England
United Kingdom
ST4 6QG

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03g47g866

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
To be confirmed at a later date

Intention to publish date
30/09/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Professor Christine Roffe.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V2.1	10/03/2017	04/09/2017	No	Yes
HRA research summary			28/06/2023	No	No