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A multicentre pragmatic clinical investigation to assess the efficacy of TransiCap MRI marker devices in magnetic resonance imaging when used to determine whole gut transit time, and inform treatment selection in paediatric constipation

Submission date
16/03/2020

Recruitment status
No longer recruiting

Registration date
02/04/2020

Overall study status
Completed

Last Edited
08/07/2024

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims

One in ten children worldwide has constipation and it becomes chronic in 30% of these children, affecting their and their families' well-being. Managing these children is difficult, partly because it can be difficult to define the nature and cause of the problem. If the doctors could send the children for a quick test that indicates the time that food takes to travel through the gut (the "gut transit time"), they could use this information to help choose the best therapy, for example to decide if a patient needs surgery. The test could also be used to follow up the effects of different treatments. Gut transit time is often not tested due to the unsuitable radiation dose involved in the current methods such as X-ray. Doctors' decisions have to rely mostly on symptoms, leading to repeated appointments, causing inconvenience for parents and children and loss of time from school and work, frustration with lack of effective treatments and consequently wasting valuable NHS resources. Researchers have devised a new way to measure gut transit time using TransiCap capsules. These capsules are swallowed by the patient, and the capsules journey through the gut is captured using Magnetic Resonance Imaging (MRI). These images can be used to measure gut transit time by counting how many capsules appear in each image. The aim of this study is to use gut transit time measurements to inform a patient's treatment, and measure whether informed treatment selection leads to treatment success at 12 months.

Who can participate?

Children aged 7-18 who have received a clinical diagnosis of constipation will be able to participate. Unfortunately, participants will be excluded from the study if they: have any history of gastrointestinal surgery, are unable to receive MRI scans, are pregnant or are planning a pregnancy, suffering from bowel stricture disease, suffering from Crohn's disease, suffering

from Hirsch sprung disease, have any congenital anorectal malformations or paediatric pseudo-obstruction syndrome, have difficulty in swallowing, or are using drugs that have an effect on gut motility such as opioids or Buscopan.

What does the study involve?
The study involves attending three hospital visits. At the first visit, the participant will consent to the study and will complete baseline assessments. The participant will be randomly allocated to either the control group or the intervention group and will be given all the questionnaires and diaries needed to be completed at home. They will also be given 72 TransiCap MRI markers to swallow over the 3 days preceding the next visit. Before the visit, participants will complete a stool diary, quality of life questionnaire and daily pain questionnaires at home.
The next visit will include an MRI scan to measure how man TransiCap MRI markers are visible in the gut. If markers are visible on the scan, the participant will attend another MRI visit 3 days later to document how many TransiCap MRI markers remain. Both images will be used by the radiologist to calculate the whole gut transit time of the participant. This will be shared with the treating clinician of participants in the intervention group only. The participants in the control group will receive standard care not informed by the TransiCap capsules. Participants have now completed the last visit and will be required to complete questionnaires at home for one more day. These are then returned to the research team. At 6 and 12 months after the MRI visits, the research team will post a one-week diary, pain score questionnaire and quality of life questionnaire to the participant for them to complete and return. Once the participant returns the questionnaires at 12 months, they have completed the study.

What are the possible benefits and risks of participating?
There are no guaranteed benefits for participating in the study. There is a chance that if gut transit time is made available to the treating clinician, intervention group participants may receive different treatment or therapy than if they might if they were not participating. This treatment may be beneficial to their condition, although there is no guarantee that this will be the case. The risks associated with participation are small. MRI is considered a relatively safe imaging technique. Some people who do not like loud noises or tight spaces may however find MRI uncomfortable. There is a small risk of aspiration or choking when swallowing TransiCap MRI Markers, although the risk is no different to when swallowing any object, such as food. To mitigate the risk, participants are encouraged to swallow the device with water or food such as yoghurt or smoothie whilst under adult supervision.

Where is the study run from?
The study is run from a number of hospitals across the UK. The study is coordinated nationally by Derby Clinical Trials Support Unit with support from the East Midlands CRN. Nottingham University Hospitals NHS Trust will provide oversight of the study in their role as the sponsor.

When is the study starting and how long is it expected to run for?
June 2019 to October 2022

Who is funding the study?
NIHR Invention for Innovation funding programme (UK)

Who is the main contact?
The main study contacts for the study are the trial manager and Chief Investigator. The trial manager and the whole Derby CTSU team can be contacted via uhdb.magic2@nhs.net, and the Chief Investigator Prof. Luca Marciani can be contacted via luca.marciaini@nhs.net

Contact information

Type(s)
Scientific

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Integrated Research Application System (IRAS)
272546

Central Portfolio Management System (CPMS)
44714

Study information

Scientific Title
A multicentre pragmatic clinical investigation to assess the efficacy of TransiCap MRI marker device in magnetic resonance imaging in paediatric constipation (MAGIC2)

Acronym
MAGIC2

Study objectives
Principal research question/objective:
To test if the use of the TransiCap MRI visible capsules to inform treatment selection leads to a change in rate of “treatment success” at 12 months after diagnosis

Secondary research questions/objectives:
1. To assess the performance of TransiCap MRI visible capsules in obtaining a measure of whole gut transit time, followed by a subsequent clinical diagnosis to inform treatment selection on the patient’s clinical condition
2. To assess the safety of the TransiCap MRI visible capsules by monitoring adverse events and

identifying any undesirable side effects
3. To assess the performance of the TransiCap MRI visible capsules system by assessing patient acceptability and procedural delivery success (usability)
4. To assess patient and carer's quality of life (performance)
5. To undertake an economic evaluation of the TransiCap MRI visible capsules cost-effectiveness

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval 09/04/2020, West Midlands – Edgbaston Research Ethics Committee (3rd Floor Barlow House, Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8193; edgbaston.rec@hra.nhs.uk), REC ref: 20/WM/0040

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Diagnosis, Device, Imaging, Management of Care

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Paediatric constipation

Interventions
This is a fully powered, multi-centre, open-label, pragmatic Randomised Controlled Trial (RCT) to test if the use of the TransiCap MRI visible capsules to inform treatment selection leads to a change in the rate of "treatment success" at 12 months after diagnosis. Two study arms will include 436 young patients that present at secondary or tertiary care with intractable constipation from across 8 UK sites.

All participants will receive the TransiCap MRI visible capsules and the MRI scans at presentation, but only the participants in the intervention arm will have the results of their scan shared with the standard care team immediately. The intervention arm will therefore receive treatment which is informed by the TransiCap MRI transit time test. The participants in the control arm will instead receive standard care not informed by theTransiCap MRI visible capsules. The results of their scans will be shared with the standard care team after the patient's follow up of 12 months is complete. All participants will receive the TransiCap capsules and the MRI scans.

Screening
Participants will be identified by secondary or tertiary care provider. The participant and carer will be provided with an age-appropriate PIS and will be given time to consider the study.
Baseline: confirm eligibility and information provision
Discussion and questions, assent and consent, baseline data collection, questionnaire completion.
The participant will stop taking medication 7 days prior to starting the questionnaire pack.
On Day 0 the participant will complete the first EQ-VAS, Stool Diary entry, EQ-5D-Y.
On Day 1 the participant will swallow 24 TransiCap capsules and complete the second EQ-VAS and Stool diary entry.

On Day 2 the participant will swallow 24 TransiCap capsules and complete the third EQ-VAS and Stool diary entry.
On Day 3 the participant will swallow 24 TransiCap capsules and complete the fourth EQ-VAS and Stool diary entry.
On Day 4 the participant will attend an MRI visit and will have an MRI scan. If no capsules are visible on the scan, the day 7 scan will be cancelled. On this day the participant will complete the fifth EQ-VAS and Stool diary entry.
On Day 5 the participant will complete the sixth EQ-VAS and Stool diary entry.
On Day 6 the participant will complete the seventh EQ-VAS and final Stool diary entry.
On Day 7 the participant will attend an MRI visit and will have an MRI scan. On this day the participant will complete the eighth EQ-VAS
On Day 8, the participant will complete an EQ 5D Y and the final EQ VAS, the carer will also complete an AC QOL. The participant will then post the questionnaire pack back to the researcher using a pre-paid envelope.
At 6 and 12 months, the participants will be followed up and will be asked to complete a 7 Day stool diary, EQ VAS, EQ 5D Y and the carer will complete an AC QoL. At these time points, researchers will complete medical notes review for all other data collection.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
TransiCap MRI visible capsules

Primary outcome(s)
Treatment success, defined as 3 or more bowel movements in one week and/or 1 or fewer episodes of bowel incontinence in one week, between the MRI-informed treatment versus standard treatment at 12 months after the final MRI visit (+/- 2 weeks). This will be measured using a patient stool diary at 12 months follow-up.

Key secondary outcome(s)
1. Number of Serious Adverse Events, measured via medical notes review at MRI visits, at 6 and 12 months follow up
2. Identification of any undesirable side effects (ADE'S) measured via medical notes review at MRI visits, at 6 and 12 months follow up
3. Number of TransiCap MRI visible capsules swallowed, collected by TransiCap questionnaire Day 1-3
4. Attendance at MRI scans measured using CRF at both MRI visits
5. Capsules visible on both scans (Intervention arm only) collected by MRI images/reports
6. Gut transit time (intervention arm only) calculated using MRI report at day 4 and day 7
7. Patient acceptability of swallowing the TransiCap MRI visible capsules (usability and acceptability performance) collected by TransiCap questionnaire on Day 1-3
8. Patient quality of life collected using EQ-5D-Y at baseline, day 0 and day 8, at 6 and 12 months follow up
9. Pain measured using EQ VAS score at baseline, day 0 – day 8, at 6 and 12 months follow up
10. Parents/carers quality of life measured using AC-QoL score at baseline, day 0 and day 8, at 6 and 12 months follow up
11. Patient symptoms (flatulence, bloating and abdominal pain) collected through patient stool

diary at day 0 – day 6, at 6 and 12 months follow up
12. Stool shape collected through patient stool diary at day 0 – day 6, at 6 and 12 months follow up:
13. Number of people completing the MRI study measured using CRF at Day 8
14. Treatment selection measured by medical notes review at 6 and 12 months follow up
15. Treatment success collected through patient stool diary at 6 months follow up
16. Gut transit time used to inform treatment selection (intervention arm only) measured using CRF at 6 and 12 months follow up:
17. Capsules visible on both scans (control arm) collected by MRI images/reports at 12 months
18. Gut transit time (hours) (control arm) measured using MRI report at 12 months

Completion date
02/10/2022

Eligibility

Key inclusion criteria
1. Children aged 7 – 18 years old
2. Able to give assent/consent or have a parent/carer able to give informed consent
3. Willing to allow his or her General Practitioner and consultant, if appropriate, to be notified of participation in the clinical investigation
4. Children diagnosed with clinical diagnosis of constipation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
7 Years

Upper age limit
18 Years

Sex
All

Key exclusion criteria
1. Female participants who are pregnant, lactating or planning pregnancy during the course of the clinical investigation. This will be self-reported
2. Any history of gastrointestinal surgery that could affect gastrointestinal function, such as colectomy or small bowel resection
3. Existing ACE procedure before the first MRI scan
4. Contraindications for MRI scanning i.e. metallic implants, pacemakers, history of metallic foreign body in eye(s) and penetrating eye injury
5. Inability to lie flat and relatively still for less than 5 minutes

6. Poor understanding of English language
7. The following disease or disorder: bowel stricture disease, Crohn’s or any difficulty in swallowing (dysphagia), Hirschsprung disease, congenital anorectal malformations, paediatric pseudo-obstruction syndrome
8. Currently using the following drugs influencing drug motility:
8.1. Opioid analgesics (tramadol, morphine, fentanyl, oxycodone, co-codamol and codydramoland)
8.2. Antispasmodic Buscopan (hyoscine butylbromide, also known as scopolamine butylbromide)
9. Participants who have participated in another research clinical investigation involving an investigational product in the past 12 weeks.
10. 4 or more bowel movements in one week and no episodes of bowel incontinence in one week (if these are reported in the participant’s medical notes. Absence of this information should not warrant exclusion)

Date of first enrolment
01/05/2020

Date of final enrolment
02/10/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Nottingham University Hospitals NHS Trust
Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield
United Kingdom
S10 2TH

Sponsor information

Organisation
Nottingham University Hospitals NHS Trust

ROR
https://ror.org/05y3qh794

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR200014

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		17/08/2020	08/07/2024	Yes	No
HRA research summary			28/06/2023	No	No