ISRCTN14173715 https://doi.org/10.1186/ISRCTN14173715

Can an enzyme-rich malt extract improve the symptoms of irritable bowel syndrome?

Submission date
23/05/2021

Recruitment status
No longer recruiting

Registration date
15/06/2021

Overall study status
Completed

Last Edited
08/07/2021

Condition category
Digestive System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Irritable bowel syndrome (IBS) is a common condition which causes symptoms of abdominal pain, bloating and altered bowel habit. Conventional treatment is frequently unsatisfactory. The cause of IBS is unknown, but it has been suggested that many of the symptoms result from undigested carbohydrates reaching the large bowel (colon). When this happens, the gut bacteria living in the large bowel can ferment undigested food, producing chemicals that cause disease. These chemicals can be detected in both blood and urine. It has been shown that reducing the number of certain carbohydrates within the diet can improve the symptoms of IBS for some patients.
This study will explore whether giving a food supplement called enzyme-rich malt extract (ERME) that contains a high concentration of enzymes that digest carbohydrates will improve the symptoms of IBS. ERME is a by-product of the malting process, in which cereal grains (like barley) are dried, commonly for making beer. It is sweet, palatable and easily available at relatively low cost and has been used as a foodstuff in baking and cookery for many years.

Who can participate?
Patients aged 18-65 years with symptoms of IBS

What does the study involve?
Following the initial screening telephone call, if the patient's IBS symptoms are suitable for the study they will be invited to attend a research clinic appointment. During this clinic visit, the study team will assess the patient's IBS symptoms, current medication regime and full medical history. Previous blood and stool tests will also be examined. If the tests have been performed more than 12 months ago, participants will need to repeat these. The tests will be performed by a member of the research team. Patients will be asked to provide a urine sample at the start and end of the study so that we can see if there are any bacterial changes in the urine.
Patients agreeing to take part in the study will be randomly assigned to take either 30 ml of enzyme-rich malt extract (ERME) each day or a similar product, also made from barley, that tastes the same but that does not contain the active ingredient (placebo). Patients have an equal chance of being allocated ERME or placebo and neither the patient nor the research team will know which arm of the study they are assigned to.
ERME is a yellow-brown syrup and 30 ml of product is about two tablespoons. Participants are

asked to take 15 ml (one tablespoon) at breakfast time, and another 15 ml (one tablespoon) with the last meal of the day, for a period of 6 weeks. The product can be spread on toast or just taken from the spoon. ERME is sweet and most patients find it very palatable. All patients will be offered an opportunity to taste the ERME product so that they are able to make a decision about whether they would find it acceptable to take.
Patients will be asked to undertake fortnightly symptom questionnaires and our research team can complete these over the telephone if required. 6 weeks after starting the study, patients will be asked to return to the research clinic for a final visit where the questionnaires will be repeated and a further urine sample requested. Patients will stop taking the ERME product at this time.
All samples taken by the research team will only be identifiable by a unique study number to maintain confidentiality throughout the study and all samples will be destroyed once the research has been completed.
Two weeks after the final clinic visit, a member of the research team will contact the patient by telephone to assess their IBS symptoms and to complete the questionnaires for the final time. After this, patient involvement in the study will be completed. Once the study is completed and the information is analysed patients will be provided with a summary of the results.

What are the possible benefits and risks of participating?
It is possible that ERME will improve the symptoms of IBS. Unfortunately, because ERME is not currently being manufactured commercially, the researchers cannot continue to provide the product to patients once the study has ended.
The researchers currently do not know of any disadvantages or risks of taking part in this study. It is possible that some patients could experience slightly looser bowel motions although we believe this is unlikely at the dose of ERME product being advised.
If patients require a repeat blood sample to confirm eligibility, this occasionally may cause some minor discomfort and slight bruising at the sampling site. If patients are required to provide a repeat stool sample the research team will explain how to perform this, provide all the necessary equipment and instruct how to return the specimen.

Where is the study run from?
Joint Clinical Research Facility, Institute of Life Sciences 2, Swansea Bay University Health Board (UK)

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

Who is funding the study?
Ateria Health Ltd (UK)

Who is the main contact?
Andrew Cunningham
cunninghamal@doctors.org.uk

Contact information

Type(s)
Scientific

Contact name
Mr Andrew Cunningham

ORCID ID
https://orcid.org/0000-0003-2686-159X

Contact details
JCRF
ILS2
Swansea University
Swansea
United Kingdom
SA2 8PP
+44 (0)1792 530819
Andrew.Cunningham@wales.nhs.uk

Additional identifiers

Integrated Research Application System (IRAS)
272652

Protocol serial number
Protocol Version 11.1

Study information

Scientific Title
Pilot study to assess the effect of an enzyme-rich malt extract in the treatment of irritable bowel syndrome

Acronym
ERME

Study objectives
The researchers wish to investigate whether ERME (an enzyme-rich malt extract) is of any benefit in the treatment of irritable bowel syndrome (IBS) patients and to seek microbiome biomarkers in urine samples, which may allow the objective identification of these patients, currently separable only by symptoms.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/12/2019, Wales Research Ethics Committee 2 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2920 785738; Wales.REC2@wales.nhs.uk), REC ref: 19/WA/0320

Primary study design
Interventional

Study design
Single-centre double-blinded randomized pilot interventional study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Irritable Bowel Syndrome (IBS)

Interventions
25 patients per treatment arm are sufficient to characterise the distribution of outcome variables which may be investigated in the definitive study. Randomisation will continue until a total of 50 evaluable subjects have been recruited (25 per study arm).

Active treatment: A total of 30 ml daily ERME (enzyme-rich malt extract).
Control treatment: A total of 30 ml daily of light malt extract that has been pretreated to destroy enzyme activity (heat-denatured malt product).

Patients with IBS will be randomised in a double-blind fashion for a pilot study to be invited to receive a 4-week course of either the enzyme-rich malt extract, used for many years in baking and cookery or a placebo. Patients will be randomised 1:1 to receive either ERME 30 ml daily in two doses (i.e. 15 ml at breakfast and 15 ml with the last meal of the day) or a control preparation (heat-denatured malt product) in the same dosage. The allocation will be double-blind (neither the patient nor the research team will be aware whether they are receiving ERME or the control preparation) and will be via the online randomisation service sealedenvelope.com.

Patients will be invited to take part in this research study after being identified through secondary clinics because they have symptoms consistent with IBS. The invitation will be followed up by an initial study screening telephone call to assess whether the patient's IBS symptoms are suitable for the study before potentially being invited to attend a research clinic appointment.

During this clinic visit, the study team will assess the patient's IBS symptoms, current medication regime and full medical history in order to satisfy eligibility. Previous blood and stool investigations will also be examined according to the study protocol. If the investigations have been performed more than 12 months ago, the study team will seek permission to repeat them. Urine samples will be requested from all eligible patients at the start and the end of the study so that microbiome alterations can be assessed by the investigative team. All samples will only be identifiable by a unique study number to maintain confidentiality and all samples will be destroyed after the research has been completed.

Patients will be asked to undertake fortnightly symptom questionnaires enquiring about specific IBS symptoms that are affecting them at that particular time. After 6 weeks, patients will be asked to return to the research clinic for a final visit where a repeat urine sample will be requested. Two weeks after the final visit a member of the research team will make telephone contact to assess patients current IBS symptoms at that time and complete a final questionnaire.

Intervention Type
Supplement

Primary outcome(s)
IBS severity measured using the IBS severity scoring system questionnaire (IBS-SSS) at the initial clinic visit and at the final clinic visit 6 weeks after initiation

Key secondary outcome(s)
IBS severity measured using the IBS severity scoring system questionnaire (IBS-SSS) at baseline (clinic visit 1), 2 weeks after initiation and 4 weeks after initiation

Measured at the initial study visit, week 2 post-initiation, week 4 post-initiation and at the final clinic visit at 6 weeks post-initiation:
1. Severity of abdominal pain measured using the IBS-SSS
2. Frequency of abdominal pain measured using the IBS-SSS
3. Abdominal bloating measured using the IBS-SSS
4. Bowel habit "satisfaction" measured using the IBS-SSS
5. Impact of IBS upon lifestyle measured using the IBS-SSS
6. Bowel frequency measured using the IBS-SSS
7. Stool consistency measured using the IBS-SSS
8. Absence from work days related to IBS measured using the IBS-SSS
9. Quality of life measured using the IBS quality of life questionnaire (IBS QOL)

Completion date
01/08/2022

Eligibility

Key inclusion criteria
1. Aged 18-65 years
2. Current symptoms of IBS (abdominal pain and altered bowel habit) ROME IV
3. Prepared to take ERME for the duration of the study (taste test available for the patient)
4. Normal full blood count (FBC) within the last 12 months. Due to the disruption caused by COVID-19, if the most recent FBC has expired, patients will be offered a repeat blood test to be performed in the research unit in order to satisfy the inclusion criteria. In the event of an abnormal test, this will be followed up by the referring Gastroenterologist. The sponsor will be covering the costs.
5. Normal calprotectin within last 12 months <50. Due to the disruption caused by COVID-19, if the faecal calprotectin has expired, patients will be offered a repeat test to be performed in the research unit in order to satisfy the inclusion criteria. In the event of an abnormal test, this will be followed up by the referring Gastroenterologist. The sponsor will be covering the costs.
6. Normal tTG (Tissue Transglutaminase) <10
7. Positive IBS subtype “malfermentation” confirmed by screening questionnaire 2
8. Registered with a GP and consent to GP being informed

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit

65 Years

Sex
All

Key exclusion criteria
1. Pregnant, planning to become pregnant or lactating
2. Diabetic (or other co-morbidity which the chief/principal investigator considers inappropriate)
3. On a restrictive diet or unwilling or unable to change diet
4. Current medication (e.g. opiates) that may influence bowel symptoms (at the discretion of the chief investigator)
5. Antibiotic treatment in the previous 6 weeks.
6. Other gastrointestinal disease (e.g. coeliac or Crohn's disease)
7. Significant gastrointestinal surgery (this will be a clinical decision and any patient who has had a surgical procedure that would change the mechanics of gut function would be excluded)
8. Involved in other gastroenterology research project or other interventional study that would affect results

Date of first enrolment
28/02/2020

Date of final enrolment
01/03/2022

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Swansea University
Joint Clinical Research Unit (JCRF)
Institute of Life Science 2
Swansea
United Kingdom
SA3 5AU

Sponsor information

Organisation
Swansea Bay University Health Board

ROR

https://ror.org/04zet5t12

Funder(s)

Funder type
Industry

Funder Name
Arteria Health Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version v3.3	07/07/2020	08/07/2021	No	Yes