ISRCTN78807934 https://doi.org/10.1186/ISRCTN78807934

Clinical trial with fermented milk drink on functional constipation

Submission date	Recruitment status	[ ] Prospectively registered
12/07/2017	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
29/08/2017	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
29/08/2017	Digestive System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Treatment options for functional constipation (FC) other than laxatives are limited. It would be therefore be useful to determine the effectiveness of other treatment options for FC that may be more widely accessible. Many subjects enquire about self-help measures, such as probiotics (live bacteria and yeasts that are good for the digestive system) to reduce the impact of FC, but at present evidence with probiotics to this end are limited. The aim of this study is to determine if consumption of probiotic dairy drink improves defecation frequency, stool consistency, bowel transit time and constipation severity compared with placebo.

Who can participate?
Men and non-pregnant women aged from 18 to 70 years who had a fewer defecations than 3 per week and were diagnosed as FC.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive either one bottle (á 65ml) of fermented milk drink containing probiotic strain to drink each day for 12 weeks. Those in the second group receive a placebo (acidified milk drink without any bacteria strains) for 12 weeks. Participants attend study visits at gastroenterologist two weeks before the start, at the start of study, then four and eight weeks after, at the end of intervention, and 4 weeks after. Participants complete quality of life and symptom questionnaires at each visit. They undergo abdominal x-ray test at the start and the end of intervention to evaluate bowel transit time. Blood and urine samples are collected before and end of the intervention for standard safety analyses. Participants keep a daily diary to record bowel movements, laxative use and food record throughout the study period.

What are the possible benefits and risks of participating?
There are no direct benefits or risks with participating.

Where is the study run from?
This study is being run by the Istituto Clinico Humanitas (Italy) and four other sites in Italy.

When is the study starting and how long is it expected to run for?
June 2012 to August 2017

Who is funding the study?
Yakult Honsha Co., Ltd. (Japan)

Who is the main contact?
Mr Cesare Mutti

Contact information

Type(s)
Public

Contact name
Mr Cesare Mutti

Contact details
Sprim Advanced Life Sciences GCP S.r.l.
Via Brisa 3
Milano
Italy
20123

Additional identifiers

Protocol serial number
13IT-1-SPRIM-CON1

Study information

Scientific Title
A double blind, randomized, controlled trial to evaluate the effects of the consumption of a fermented milk drink on bowel function in adults

Study objectives
The aim of this study is to determine if consumption of fermented milk drink containing a probiotic strain improves bowel movement frequency in adults with functional constipation (FC), as determined via the change in the numbers of complete spontaneous bowel movements (CSBMs) during consumption for 12 weeks.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethic Committee IRCSS Istituto Clinico Humanitas, 25/07/2014, ref: Prot. Nr. CE Humanitas ex D. M. 8/2/2013 - 246/2014

Primary study design

Interventional

Study design
Interventional multicentre randomised double-blind placebo-controlled trial

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Gastrointestinal-Functional Constipation

Interventions
Participants are randomly allocated to receive either one bottle (á 65ml) of fermented milk drink containing probiotic strain per day or placebo (acidified milk drink without any bacteria strains) for 12 weeks. Randomisation is done per study centre using Latin-square design, using gender and the number of CSBMs at week -1 as determining factor.

Participants attend study visits at gastroenterologist in two weeks before the start, at the start of intervention, then 4 and 8 weeks after, at the end of intervention, and four weeks after. Participants complete quality of life and symptom questionnaires at each visit. They undergo abdominal x-ray test at the start and the end of intervention to evaluate bowel transit time. Blood and urine samples are collected before and end of the intervention for standard safety analyses. Participants keep a daily diary to record bowel movements, laxative use and food record throughout the study period.

Intervention Type
Supplement

Primary outcome(s)
Number of CSBMs is measured using patient daily diary at week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12.

Key secondary outcome(s)
1. Number of spontaneous bowel movements (SBMs) per person is measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
2. Number of participants with at least one CSBM improvement per week is measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
3. Number of SBMs per person is measured using daily diary at Week 12, and compared with the number at the baseline (Week -1)
Absolute weekly SBM counts are measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
4. Number of patients with at least one SBM improvement per week is measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
5. Number of participants with at least three CSBMs per week is measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
6. Number of participants with at least three SBMs per week is measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
7. Number of persons having at least an increase of +1 CSBM for at least 6 weeks during the 12 weeks is measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
8. Stool form is measured using Bristol Stool Scale Form in the daily diary at Week one, two,

three, four, five, six, seven, eight, nine, ten, 11 and 12
9. Abdominal transit time is measured using radio opaque markers at Week zero (at start of the intervention) and Week 12
10. Number of participants who used laxatives once or more during the intervention is measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
11. Frequency of using laxatives is measured using daily diary at Week one, two, three, four, five, six, seven, eight, nine, ten, 11 and 12
Tertiary Endpoints:
I. Change in constipation symptoms measured by PAC-SYM questionnaire during the intervention.
II. Change in quality of life measured by PAC-QOL questionnaire during the intervention.

Completion date
03/08/2017

Eligibility

Key inclusion criteria
1. Males and non- pregnant females aged from 18 to 70 years
2. Body mass index (BMI) >18.0 and <30 kg/m2
3. Diagnosed as a subgroup of functional constipation, fulfilling Rome III criteria for functional constipation and have a defecation frequency of <3 SBMs per week with a diagnosis of >3 months and with symptom onset at least 6 months before diagnosis at the screening visit V0. Subjects are required to have BM frequency <3 CSBMs per week at the baseline visit V1 during the 2 weeks before randomization.
4. Agree to avoid using any laxative during the baseline period and the study period except in the case the investigator allows him/her to have rescue medication
5. No use of laxatives within 15 days before baseline
6. No consumption of forbidden foods in the previous 30 days before V0 (according to the list of forbidden foods A)
7. Ability of the participant (in the investigator’s opinion) to comprehend the full nature and purpose of the study including possible risks and side effects
8. Consent to the study and willing to comply with study product and method
9. Agree not to alter their diet in any way for the duration of the trial and to maintain it at steady state (according to the forbidden food list) and not to make any major lifestyle changes (e.g. changing their exercise pattern) during the trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Neurological, pharmacological or organic cause for constipation
2. Subjects with 3 or more CSBMs at week -2 or at week -1
3. Habitual users of laxatives, since 3 months before enrolment
4. Major neurological disease or injury (e.g. Multiple sclerosis, Spinal Cord Injury - SCI)
5. Major gastrointestinal complication (e.g. Crohn's disease, colitis, celiac disease, lactose intolerance and allergy to cow-milk proteins).
6. Febrile diverticulitis within 1 year before enrolment
7. Prior abdominal surgery of the following type: gastric bypass, lap band, colectomy, except appendectomy, haemorrhoidectomy and cholecystectomy
8. Any subject who on first assessment has symptoms requiring urgent medical assessment or treatment (e.g. rectal bleeding which requires endoscopy)
9. Any subject that present abdominal pain as a predominant symptom
10. Any subject that need manual maneuvers (digital insertion into the rectum, perianal pressure or vaginal splinting) to evacuate stools.
11. Any subject presenting a condition that constitutes a contraindication to probiotics (e.g. immunosuppressed, active current sepsis, untreated carcinoma)
12. Any subject presenting any alarm symptoms or situation requiring as a recommended test a colonoscopy (according to WGO Global Guideline Constipation 8, World Gastroenterology Organization, 2010)
13. Pregnancy and expected pregnancy within coming 18 weeks
14. Antibiotic use in the previous 12 weeks
15. Use of drugs or alimentary supplements known to cause constipation
16. Subjects who do not have the capacity to consent
17. Anticipated major dietary or exercise changes during the study period
18. Subjects known to exceed in the consumption of the following foods, for example due to dietary reasons: yogurt, cheese, soy/rice or other products only containing L. bulgaricus and S. thermophilus as viable bacteria; fermented milks, cheese, soy/rice products and other dairy/non-dairy products containing unknown viable bacteria or different from probiotic bacteria; foods naturally rich in prebiotics
19. Known allergies to any substance in the study product
20. Eating disorder (anorexia, bulimia, binge eating disorder, obesity)
21. History of alcohol, drug or medication abuse
22. Participation in another study with any investigational product within 3 months before enrolment
23. Investigator believes that the participant may be uncooperative and/or noncompliant and should therefore not participate in the study

Date of first enrolment
17/11/2014

Date of final enrolment
13/04/2017

Locations

Countries of recruitment
Italy

Study participating centre
Istituto Clinico Humanitas
Via Manzoni 56
Milano
Italy
20089

Study participating centre
Fondazione IRCCS – Policlinico San Matteo
Viale Camillo Golgi 19
Pavia
Italy
27100

Study participating centre
A.O. Spedali Civili di Brescia
Piazzale Spedali Civili 1
Brescia
Italy
25123

Study participating centre
Az. Ospedaliera per l'Emergenza Cannizzaro
Via Messina 829
Catania
Italy
95126

Study participating centre
A.U.O. Policlinico G. Martino
Via Consolare Valeria 1
Messina
Italy
98125

Sponsor information

Organisation
Yakult Honsha Co. Ltd

ROR
https://ror.org/03wmnrc91

Funder(s)

Funder type
Other

Funder Name
Yakult Honsha Co. Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study is not expected to be made available due to at the start of the trial project in 2012 it was not planned to make the raw data available and the Informed Consent Form was not designed for it either. Therefore some additional arrangements are needed to make the datasets, which will be held by the Sponsor, available. If there is the necessity and on reasonable request, however, we would consider about it. Electronic records of subjects Clinical Study Data is User Privileged and password protected EDC Platform in accordance with USFDA 21 CFR Part 11 guidelines. Final Dataset will be arranged in SAS file.

IPD sharing plan summary
Not expected to be made available