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Effects of milk proteins on gut and stomach symptoms

Submission date	Recruitment status	[X] Prospectively registered
28/06/2019	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/07/2019	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
02/12/2020	Digestive System	

Plain English summary of protocol

Background and study aims
Functional gastrointestinal disorders such as Irritable bowel syndrome (IBS), functional dyspepsia /bloating and functional diarrhea are common, long-term conditions that affect the digestive system. The symptoms can vary greatly from person to person but typical symptoms include abdominal pain, bloating, diarrhea, gas and stomach rumble. The exact cause of functional symptoms are not known. However, many think that symptoms are related to hypersensitive gut and stomach, and that foods play major role in triggering symptoms. There is no cure for functional gastrointestinal disorders but dietary changes can help to ease the symptoms. The role of lactose in inducing gut and stomach symptoms in lactose intolerant people is widely known. However, the role of milk proteins, casein and whey, is poorly understood. Some people with sensitive gut and stomach report that milk and other dairy products commonly trigger symptoms; it is possible that proteins trigger these symptoms. Early studies have suggested that hydrolyzed milk protein might be better tolerated than intact milk protein. The aim of this study is to compare the effects of regular milk protein to hydrolyzed milk protein in people with sensitive stomach and gut, i.e. in functional gastrointestinal disorders.

Who can participate?
People aged 18-65 who have at least one of the following functional gastrointestinal disorders: irritable bowel syndrome, functional dyspepsia/bloating or functional diarrhea

What does the study involve?
The study involves two separate 10-day test periods which are spaced at least 10 days apart. One involves eating partially hydrolyzed milk products and the other involves eating regular milk products; both products are chocolate milkshakes and they are provided for free. The diet is meant to be otherwise as normal as possible. The participants take part in both test periods but they are taken in a random order. At the beginning and end of each test period participants give a blood and urine sample and answer questions related to stomach and gut symptoms. Over the following 10 days, participants are asked about symptoms they are having. At the end of the study, the participants are entitled to approximately 30 min dietitian consultation given by the designated study dietitian. Participants can withdraw from the study at any time point.

What are the possible benefits and risks of participating?
There are no direct benefits of taking part, although participants are able to receive information about the state of their health. Risks of participating include the possibility that milk protein products induce stomach and gut symptoms.

Where is the study run from?
Valio Oyj Ltd

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

Who is funding the study?
Valio Oyj Ltd

Who is the main contact?
Dr Reijo Laatikainen

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
76

Study information

Scientific Title

Effects of milk protein hydrolysis on gastrointestinal symptoms in functional gastrointestinal disorders: a randomized controlled trial

Acronym
SILKY II

Study objectives
Partially hydrolysed dairy protein is better tolerated in functional gastrointestinal disorders than intact dairy protein.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/05/2019, ethics committee of the Hospital District of Helsinki and Uusimaa (HUS keskuskirjaamo, Tynnyrintekijänkatu 1C, 00290 Helsinki, Finland; Tel: +358 (0)9 4711 (ask to connect to ethics committee); Email: eettiset.toimikunnat@hus.fi), ref: HUS/576/2019

Study design
Single-centre double-blind cross-over randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Functional gastrointestinal disorders including irritable bowel syndrome, functional dyspepsia /bloating and functional diarrhea

Interventions
Participants receive the 10-day intervention and 10-day control treatment in a random order, which are delivered at separate study visits (wash out at least 10 days apart). At baseline, participants give a blood sample, an overnight urine sample and respond to IBS-SSS questionnaire.

Intervention: Participants will be given hydrolysed milk protein products (milkshakes) for daily consumption, equivalent to approximately 50 grams protein per day. Otherwise, the participants continue on their habitual diet.
Control: Participants will be given regular milk protein products (milkshake) for daily consumption, equivalent to approximately 50 grams protein per day. Otherwise, the participants continue on their habitual diet.

In each condition, at the beginning and at the end of each treatment period, i.e. control and intervention period, blood and urine samples are collected and symptoms are monitored on daily basis.

Intervention Type
Other

Primary outcome(s)
1. Gastrointestinal symptoms measured by IBS-SSS scoring system (Francis et al. 1997) at baseline and at the end of each treatment period
2. Abdominal pain, borgorygmia, intestinal gas and bloating evaluated on 4-point Likert scale daily

Key secondary outcome(s))
1. Markers of immune activation/low-grade inflammation: e.g.IL-6, IL-1B and TNF-alfa from plasma using high-sensitivity ELISA kits and methylhistamine from overnight/12 h urine samples also using ELISA
2. Markers of intestinal permeability: FABP-2 from plasma using ELISA

All biomarkers are measured at the beginning and the end of each 10-day treatment period

Completion date
11/11/2019

Eligibility

Key inclusion criteria
1. Aged between 18 and 65 years
2. Irritable bowel syndrome, functional dyspepsia/bloating and functional diarrhea (all defined by Rome IV criteria)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
41

Key exclusion criteria
1. Organic gastrointestinal disease such as Crohn's disease, ulcerative colitis, colorectal or gastric or any cancer
2. Pregnancy or breastfeeding
3. Significant abdominal surgery (e.g. bowel resection)
4. Difficult to treat constipation
5. Medication that affects intestinal motility and/or pain perception

Date of first enrolment
05/08/2019

Date of final enrolment
01/10/2019

Locations

Countries of recruitment
Finland

Study participating centre
Booston Oy Ltd
Viikinkaari 6
Helsinki
Finland
00780

Sponsor information

Organisation
Valio Oyj Ltd

ROR
https://ror.org/00yb5c421

Funder(s)

Funder type
Industry

Funder Name
Valio Oyj Ltd

Results and Publications

Individual participant data (IPD) sharing plan
For commercial reasons the developer of the milk protein products is not ready to make the data freely available. The data will be kept at the premises of development and research department in Valio Oyj Ltd.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	18/07/2020	02/12/2020	Yes	No