A Multi-centre, Randomized, Placebo-Controlled, Efficacy Study of Prebiotic Galacto-oligosaccharides on Gastrointestinal Symptom Severity in Patients with Irritable Bowel Syndrome

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Primary Objective:To establish the efficacy of treatment with Bimuno on total IBS symptom severity in patients with IBSSecondary Objectives:To assess efficacy of treatment with Bimuno on (I) abdominal pain, (II) bloating, (III) global IBS...

Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON51897

Source
ToetsingOnline

Brief title
GOS to Reduce Symptom Severity in IBS

Condition

- Gastrointestinal signs and symptoms

Synonym
Irritable Bowel, Irritable Bowel Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Clasado Research Services Ltd
Source(s) of monetary or material Support: De Sponsor: Clasado Research Services Ltd

Intervention

Keyword: Galacto-oligosaccharides (GOS), Irritable Bowel Syndrome (IBS), Symptom Severity

Outcome measures

Primary outcome

The difference in total IBS symptom severity between treatment arms as measured by mean composite IBS Symptom Severity Scale scores at the end of the study (Day 56)

Secondary outcome

I. The difference in abdominal pain between treatment groups as measured by the mean abdominal pain symptom scores during the intervention period.

II. The difference in bloating between treatment groups as measured by the mean bloating symptom scores during the intervention period.

III. The difference in global IBS improvement between treatment arms as measured by the mean IBS Global Improvement Scale scores during the intervention period.

IV. The difference in stool consistency between treatment arms, per subtype of IBS**, as measured by the median Bristol Stool Form Scale stool type during the intervention period.

V. The difference in defecation frequency between treatment arms, per subtype of IBS**, as measured by the mean patient-reported defecation frequency during the intervention period.

VI. The difference in quality of life between treatment arms as measured by the mean composite IBS Quality of Life scores at the end of the study (Day 56).

VII. The difference in anxiety and depression between treatment arms, evaluated separately using the mean IBS Hospital Anxiety and Depression Scale scores at the end of the study (Day 56).

VIII. Nature, incidence, frequency, severity of adverse events/serious adverse events and relationship to the study intervention.

IX. Compare the need and usage of rescue medication (anti-diarrheal medication or laxatives) between the 2 treatment arms during the treatment period.

Study description

Background summary

Irritable bowel syndrome (IBS) is a highly prevalent and multifaceted functional bowel disorder characterized by recurrent abdominal pain associated with defecation or a change in bowel habits in the absence of detectable structural and biochemical abnormalities (Rome IV Criteria). Disordered bowel habits are typically present, such as constipation, diarrhoea or a mix of constipation and diarrhoea, as are symptoms of abdominal bloating/distension. The chronic and bothersome nature of IBS symptoms negatively affects patient quality of life and introduces a substantial economic burden on patients and the healthcare system. The gut microbiota composition and function may play a pivotal role in the pathogenesis of IBS, as a reduction in endogenous bifidobacteria, lactobacilli, and Faecalibacterium prausnitzii concentrations, as well as small bowel bacterial overgrowth have been reported in IBS patients, thereby introducing the gut microbiota as a potential target for treatment and symptom relief. Intervention with non-digestible food ingredients, such as galacto-oligosaccharides (GOS), may form a suitable intervention strategy, as these *prebiotics* are known to modulate the gastrointestinal (GI) microbiota and support health and wellbeing of the host. The safety and efficacy of GOS has previously been evaluated in patients with IBS, which demonstrated that GOS may reduce IBS symptom severity, improve quality of life, improve stool consistency and defecation frequency and alter gut microbiota composition, in a safe manner. As there are currently limited suitable medical treatments for IBS, this study will evaluate the efficacy of Bimuno, a dietary supplement with

GOS, in reducing symptom severity of patients with IBS.

Study objective

Primary Objective:
To establish the efficacy of treatment with Bimuno on total IBS symptom severity in patients with IBS

Secondary Objectives:
To assess efficacy of treatment with Bimuno on (I) abdominal pain, (II) bloating, (III) global IBS improvement, (IV) stool consistency, (V) defecation frequency, (VI) quality of life, (VII) anxiety and depression, (VIII), safety of treatment with Bimuno, as well as the use of (IX) rescue medication, in patients with IBS.

Exploratory Objectives:
To assess the effect of treatment with Bimuno on (A) immune function, (B) gut microbiome composition, (C) blood metabolites, (D) the correlation between blood metabolites and gut microbiome, and (E) the correlation between gut microbiome and total IBS symptom severity.

Study design

This is a Phase III, randomized, double-blind, placebo-controlled, multicenter, 8-week intervention study, preceded by a 2-week run-in period, to assess the efficacy of Bimuno on symptom severity in adult patients with IBS.

Intervention

All patients in this study will complete a 2-week run-in period without intervention and will then be matched 1:1 to receive 8 weeks of intervention with either Bimuno or placebo (double-blind):

- Active treatment: A single daily dose of 1.8 grams of Bimuno, containing 1.37g of GOS, provided as soluble powder.

- Placebo: A single daily dose of 1.8 grams maltodextrin, matching in taste, smell, appearance, and solubility, but without active ingredients (i.e. GOS).

Study burden and risks

The burden and risks of participating in the present study are low. The study procedures form little risk for patients but may burden them. Blood and faeces samples will be collected at 2 timepoints. Quantitative and qualitative data

collection does not burden patients in any other way than time spent. There will be no costs for patients for treatment and sample collection and patients will be reimbursed for associated travel expenses. Potential benefits of consumption of Bimuno include reduced IBS symptom severity, improved QoL, improved stool quality and defecation frequency, and reduced anxiety.
The consumption of both study products is considered safe and without risks. Bimuno is marketed as a food supplement since 2007, has Generally Recognized As Safe (GRAS) status for use in adults (GRN000484, FDA, 2013) and infants (GRN000495, FDA, 2013) and has a long history of safe use. Recent safety studies have concluded that the consumption of prebiotics, including GOS, is well-tolerated and safe (Davani-Davari et al., 2019; Al-Sheraji et al., 2013). Moreover, previous clinical studies with Bimuno in IBS patients were not associated with any health risks (Wilson et al., 2020; Silk et al., 2009). However, adverse events related to consumption of GOS may include minor GIT complaints, such as stomach sensitivity, flatulence, rumbling, diarrhoea, and nausea. No health risks are associated with the consumption of the other ingredients in Bimuno, i.e. glucose, galactose, lactose. Furthermore, no health risks are associated with the ingredients in placebo (maltodextrin).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Patients who have been diagnosed with IBS by a medically trained person/Health Care Professional (HCP).
2. IBS diagnosis to be confirmed according to the Rome-IV criteria by a primary or secondary care clinician, including a gastroenterologist, at study entry
3. An IBS Symptom Severity Scale score of >=125 points at baseline (V1)
4. Male or female between 18 and 64 years of age (age ranges included)
5. Possession of a smartphone
6. Willing and eligible to provide consent and comply with protocol and product intake.

Exclusion criteria

1. Unclassifiable IBS (IBS-U) as determined by Investigator
2. Use of products marketed as prebiotics, probiotics or synbiotics within 4 weeks prior to study entry (e.g. Yakult, Actimel, Activia, VSL#3, Kefir).
o Regular cheese or yogurt containing lactic acid bacteria are not an exclusion criterion.
3. Systemic antibiotic or antimycotic treatment within 4 weeks prior to study entry
4. Use of laxatives or antidiarrheal medication within 1 week prior to study entry
5. An unstable antidepressant/antipsychotic treatment regimen within 3 months prior to study entry (i.e. treatment should be stable for at least 3 months prior to study entry).
6. Confirmed lactose intolerance, defined as patients who report response to dietary elimination of lactose/dairy products. Confirmation is patient-reported and not done within the scope of this study.
7. Confirmed food allergy, with reported confirmation based on OFC, IgE, or skin prick test. Confirmation is patient-reported and not done within the scope of this study.
8. Galactosemia (galactose metabolism disorder)
9. Following diets likely to affect study outcomes, including:
o low FODMAP, KETO/high-fat, gluten free/coeliac, paleo, weight loss, caloric restriction, low-carb, 5:2/whole day energy restriction, Atkins/high-protein, sugar-free, single-food, juicing/any day of juicing, any other restriction diet (e.g. very low calory), or vegan diets (GOS is derived from cow*s milk).
10. Severe illness(es) or medical condition(s), including gastrointestinal

pathologies:
o GI ulcers, coeliac disease, inflammatory bowel disease, bowel cancer, bowel resection, , bariatric surgery, acute or chronic diarrhoea secondary to confirmed infectious gastroenteritis, or enteral or parenteral nutrition.
11. Subjects suffering from auto-immune disorders (e.g. Rheumatoid Arthritis, Systemic lupus erythematosus, Multiple Sclerosis, Graves* Disease) that require treatment with an immune modulator treatment or anti-inflammatory medication
12. Surgical operations to the mouth or gastrointestinal tract within 4 weeks prior to study entry, or planned during the study
o Appendectomy within 6 months prior to study entry
13. Recent unintended weight loss:
o >5% of total body weight within 6 months prior to study entry
14. Excessive alcohol consumption (>14 units per week) and/or drug abuse
15. Pregnancy and lactation, or plan to become pregnant during the study period
16. Participation in other studies involving investigational or marketed products concomitantly or within 3 months prior to study entry
17. Changes in diet, supplement or medication use likely to affect study outcomes (i.e. medication that influences GI function) within 4 weeks prior to study entry or planned during the study (at the discretion of the Investigator). For example, the following medications will influence GI function and changes must be avoided: opioids, prokinetics (domperidone, metoclopramide, prucalopride), antispasmodics (peppermint oil, buscopan), and acid suppressants (PPI, H2 blockers). Of note: the intake of fibres (e.g. psyllium husk) may be used provided that the participant has been using this as a supplement for more than 4 weeks prior to study participation and intake does not change during the course of participation.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	26-10-2021
Enrollment:	21
Type:	Actual

Ethics review

Approved WMO Date:	12-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL76170.056.21
Other	NL9317