Effect of Galacto-Oligosaccharides supplementation on amoxicillin-treated gut microbiota from healthy adults : a proof of principal study

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To explore whether the promising effects of GOS supplementation on the composition and activity of gut microbiota from healthy adults as found by in-vitro, can also be observed in-vivo.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal infections
Study type	Interventional

Summary

ID

NL-OMON39559

Source
ToetsingOnline

Brief title
GOS-AMX Study

Condition

- Gastrointestinal infections

Synonym
microbiota activity, Microbiota composition

Research involving
Human

Sponsors and support

Primary sponsor: Wageningen Universiteit

Source(s) of monetary or material Support: Carbohydrate Competence Centre ,FrieslandCampina

Intervention

Keyword: Antibiotic, Healthy adults, Human gut microbiota, Prebiotic

Outcome measures

Primary outcome

The primary outcome is to compare the trends from the in-vivo study to the trends from the parallel in-vitro study regarding the microbiota composition and the microbiota activity.

• Microbiota composition : amount of Bifidobacteria, Lactobacillus and Enterobacteriaceae in the faecal samples

• Microbiota activity : amount of SCFA and remaining GOS in the faecal samples

Secondary outcome

The secondary outcome is to follow up the gastrointestinal symptoms (flatulence, consistency and frequency of faeces, incidence of diarrhoea) of faeces in the in-vivo study.

Study description

Background summary

Prebiotics are thought to be a potential means to prevent antibiotic-associated diarrhoea because of their ability to stimulate beneficial bacteria. In-vitro results showed a promising recovery of Bifidobacteria combined with an increase of Short Chain Fatty Acids (SCFA) upon Galacto-oligosaccharides (GOS) supplementation to amoxicillin-treated microbiota. As the microbiota is nowadays considered as a key factor in human health, a further understanding of the gut microbiota functioning in-vivo is essential. This understanding of the use of specific prebiotics may possibly be beneficial in the prevention or recovery of antibiotic-disturbed microbiota. As the effect of GOS

supplementation in healthy adults receiving amoxicillin have never been tested in-vivo, we propose the current study as a proof of principle. The main aim of the study is to investigate changes in microbiota composition and -activity of persons having received antibiotics with/without GOS as compared to the baseline rather than investigating the occurrence of diarrhoea

Study objective

To explore whether the promising effects of GOS supplementation on the composition and activity of gut microbiota from healthy adults as found by in-vitro, can also be observed in-vivo.

Study design

Double blind randomized parallel intervention study comprising two weeks intervention and two weeks of follow up. Fecal samples will be collected on 8 occasions : at screening, day 0, day 2, day 5, day 8, day 12 day 19 and day 26. Fecal samples at day 0 will be used to perform the in-vitro parallel study.

Intervention

All subjects will receive amoxicillin (375 mg 3x per day) for 5 days. Group 1 receives a drink with GOS (2,5 g 3x per day) and group 2 receives a drink with placebo (Maltodextrine 2,5 g 3x per day) simultaneously to the antibiotic for 5 days and after the antibiotic treatment for another 7 days, 12 days in total. The intervention products should be consumed at breakfast/lunch/dinner.

Study burden and risks

This intervention is non-therapeutic to the subjects. The risk associated with participation and the burden are considered low but present. At screening, an inclusion questionnaire is filled out and height and weight are measured. Subject still have the opportunity to drop-out before starting the study. During the study, antibiotic treatment and GOS or placebo supplemented to a drink are taken for 5 and 12 days, respectively, at home during breakfast, lunch and dinner. Eight faecal samples will be collected and will be picked up at home by the researchers. Delivery of faecal samples can be 1 day after the indicated date. After the treatment, the subjects will be followed up for two weeks to check whether they feel as healthy as before the study. Amoxicillin is a marketed drug commonly used for the treatment of infections. Like all medicines, the study drug may cause side effects, but side effects are usually mild and transient in nature, nausea and diarrhoea being the most common ones. The risk for serious adverse events is considered to be lower in healthy adults as their microbiota is mature/diverse and stable as compared to infant or elderly. The healthy volunteers keep a diary and are being monitored at each required faecal donation for adverse events. Subjects will be withdrawn

from the study when diarrhoea is occurring and be followed by a general practitioner.
Although subjecting healthy people to antibiotics is considered to be undesired due to possible side effects, we felt that we did not have another choice. The option to recruit adults needing antibiotic treatment due to a minor infection was not optimal as we considered the lack of a baseline observation and faecal sample, the diversity of treatment regarding dose and duration as prescribed by the practitioner and the rush in getting started (no real time to inform the volunteer properly) as limiting factors to have a good, representative and volunteer-friendly study. In addition, using healthy volunteers in antibiotic studies using amoxicillin has been reported before. Finally, risk for diarrhoea that exist for healthy adult receiving amoxicillin treatment are defined as *nuisance diarrhoea*, which is a frequent loose and watery stools with no other complications. Risk for colitis, which is a potential source of serious progressive disease, is rare (< 0,01%).
Prebiotic GOS is known to be safe and food-grade. Possible side-effects may be bloating and flatulence but these effects are harmless and not likely to happen with 7.5g/day GOS intake.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age: 18-40
• BMI: 18.5-25 kg/m2
• Stable weight over the last 6 months
• Western diet
• Availability of information about birth by caesarean section and breast-feeding at age 0-3 months
• Regular defecation (~1day)
• Healthy as judge by the participant himself
• Having signed the informed consent form

Exclusion criteria

• Smoking or drug use
• Pregnant (include planning to be or gave birth in the last 6 months) or lactating woman
• Using contraceptive pill
• Gastro-intestinal diseases by the volunteer him/herself or in his/her family (e.g. irritable bowel syndrome, inflammatory bowel disease)
• Traveling to an Asian, African or south American country < 6 months before the study
• Hypersensitivity or food allergy for products used in this study (e.g. Lactose, Penicillin)
• History of pre-existing allergies, such as asthma and hay fever
• Having hepatic disease and renal failure
• Using medication other than paracetamol, acetylsalicylic acid (aspirin), hay fever, asthma
• Not willing to have the family doctor be informed about participation to the study
• Antibiotic use < 3 months before the study
• More than 3 antibiotic treatments in the last 2 years.
• Probiotic or prebiotic use < 1 month before the study*

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-05-2013
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	24-04-2013
Application type:	First submission
Review commission:	METC Wageningen Universiteit (Wageningen)

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	NL42438.081.12