Lactobacillus casei Shirota for influencing the microbiome of patients with Barrett's esophagus.

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Primary objectivesTo study if LcS can colonize the esophagus of BE patients.To study the effect of LcS colonization on the Gr+ (except for LcS)/ Gr- bacterial ratio of the esophagus.Secondary objectivesTo quantify the number of specific pathogenic...

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

Summary

ID

NL-OMON43164

Source
ToetsingOnline

Brief title
The Yakult study

Condition

- Gastrointestinal conditions NEC

Synonym
Barrett's esophagus

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Yakult Nederland B.V.

Intervention

Keyword: Barrett's esophagus, Lactobaccillus casei Shirota, Microbiome, Yakult

Outcome measures

Primary outcome

1. Amount of LcS bacteria (16S rDNA analysis)

2. Bacterial Gr+/Gr- ratio in the esophagus (both in BE and in squamous epithelium) (16S rDNA analysis of the esophageal flora (with and without LcS)).

Secondary outcome

3. Amount of pathogenic bacteria i.e. Campylobactor spp, Veilonella spp, Neisserria spp (16S rDNA sequencebased metagenomic analysis).

4. Immunological response to the change in microbiome (Micro-array based analysis of the expression profiles of immune responses gene).

5. Presence of inflammation (endoscopic observation).

Study description

Background summary

Barrett*s esophagus (BE) is a premalignant condition, in which the normal squamous epithelium is replaced by intestinal epithelium. BE is the most important risk factor for the development of esophageal adenocarcinoma (EAC). EAC has very low survival rates; a 5-year survival of 25% for non-metastatic disease and a 2-year survival of 9% for metastatic disease.
The most important risk factor for developing BE is gastro-esophageal reflux disease (GERD). It is believed that the abberrant chronic immune response in BE leads to the induction of dysplasia and finally EAC. Comparison of the microbiome of healty individuals, GERD patients and BE patients has resulted in the finding that BE was associated with a microbiome containing more Gr- bacteria compared to healthy individuals and GERD patients. In contrast to Gr+ bacteria, Gr- bacteria carry large numbers of lipopolysacharides (LPS) in their cell wall, and LPS molecules are strong stimulators of the Th2 immune response. The observation of an increased load of Gr- in previous studies has led to the

hypothesis that there is a potential contribution of these Gr- bacteria to the chronic inflammatory response in BE by activating the LPS/TLR4/NF-kB pathway. Restoring the Gr+/Gr- bacterial ratio with Lactobacillus casei Shirota (LcS) may revert the activation of the pro-inflammatory pathway and reduces the risk of neoplastic progression. Earlier studies with LcS have suggested that the LcS bacterium may be capable of influencing the environment in the esophagus.

Study objective

Primary objectives
To study if LcS can colonize the esophagus of BE patients.
To study the effect of LcS colonization on the Gr+ (except for LcS)/ Gr- bacterial ratio of the esophagus.

Secondary objectives
To quantify the number of specific pathogenic bacteria
To explore the effect of restoration of the Gr+/Gr- bacterial ratio on the Th1/Th2 response and the associated cytokines
To explore a change in the clinical endpoint inflammation as seen during endoscopy

Study design

The study is a single-arm, interventional pilot study to investigate the possibility of changing the esophageal microbiome by ingestion of a fermented milk drink containing LcS in patients who undergo Barrett surveillance at het Radboud University Medical Center, Nijmegen.
The study will be introduces to the patients by the treating physician. The actial inclusion will be performed by the research physician who will further inform the patients. Informed consent is signed in the presence of the research physician.

At baseline (day 0) patients will undergo an endoscopy with biopsy sampling. Besides from the biopsies needed for histological evaluation as standard care, biopsies for study purposes will be taken.
Subsequently the intervention period of 4 week starts (day 1-28). Patients will be drinking two 65ml bottles per day of Yakult, a fermented milk drink containing at least 6.5*10^9 LcS bacteria. During the intervention period, patients will not take any (other) probiotics. If a patient needs antibiotic therapy, they will be excluded from the study. The intervention period will be continued until the last evening prior to the endoscopy.
After the intervention (day 29), all patients will again undergo an endoscopy for the collection of biopsies (6 from BE, 6 from squamous epithelium).

Intervention

Patients will be drinking 2 bottles per day of a LcS containing drink (Yakult), for a period of 4 weeks.

Study burden and risks

The risks associated with participation are considered to be negligible.

Patients who will participate in the study will undergo two endoscopies with biopsy sampling.The first endoscopy is part of the routine surveillance programme (standard care). Additional biopsies will be collected for study purposes, this will extend the procedure for 5 minutes.Taking biopsies is associated with a very low risk of secondary bleeding or perforation. Therefore, the risk of taking additional biopsies is considered to be minimally increased.
The second endoscopy is not standard care. However, the risk of an endoscopy is considered extremely low. Complications are rare during and after upper ensdoscopy (1-2 : 1000 patients). The most common complain after the procedure is a sore throat. Major complications such as an upper gastrointestinal bleeding and perforation are rare (0.1% and 0.0001%, respectively).

During the intervention period, Yakult will be supplemented to the diet of the patients. Yakult is commercially available since 1994 in the Netherlands and no adverse events have been reported with the consumption of this product by healthy volunteers. Furthermore, there is no report on complications of the consumption of Yakult by BE patients. Given the fact that both Yakult consumption and BE are common in the Western countries, it is safe to assume that if such an adverse effect existed, it would probably have been noticed already.

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 years
Histopathological proof of Barrett's esophagus (BE) without dysplasia
BE length of >2 cm (C2Mx)
Signed informed consent

Exclusion criteria

Probiotic use within the last 3 months before baseline.
Antibiotic use within the last 2 months before baseline.
Infection in the oral cavity.
Esophagitis according to the Los Angeles classification (gr. A-D)
Immunocompromised patients; HIV-infection, systemic immunosuppression therapy
Patients with diabetes mellitus
Previous gastric/esophageal surgery, which has changed esophageal anatomy
Other coexistent esophageal disease (e.g. varices)
Patients with bleeding disorders
Other situations that contraindicate gastroscopy

Study design

Design

Study type: Interventional
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-04-2017
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	27-03-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 25973
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL59072.091.16
OMON	NL-OMON25973