Effect of food additive E171 (titanium dioxide) on the development of colorectal cancer, an early biomarkers research.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON54542

Source
ToetsingOnline

Brief title
E171 and colon cancer

Condition

- Gastrointestinal inflammatory conditions

Synonym
colon inflammation, gut inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W, Nederlandse Voedsel en Warenauthoriteit (NVWA)

Intervention

Keyword: Biomarker, E171, Gut inflammation, Titanium dioxide

Outcome measures

Primary outcome

The primary outcome parameters are differences in transcriptomic markers after consumption of food additive E171. These outcomes in humans will demonstrate if the intake of E171 in humans results in changes in molecular processes that are associated with increased colorectal cancer risk.

Secondary outcome

Secondary outcome parameters include inflammatory markers such as ROS in the rectal epithelium. These outcomes will help to understand the inflammatory mechanisms that may be indicative of the risk to developing colorectal cancer.

Study description

Background summary

The food additive E171 (titanium dioxide) is present at significant levels mainly in sweets, cookies, icing and chewing gum. Consumers are exposed between 1 and 2 mg/kg bw/day depending on the age, it is important to evaluate the potential risk of this compound on human health. E171 comprised titanium dioxide (TiO_2) particles of various sizes, among others in the nanoparticle size range. TiO_2 is not considered genotoxic, but in an animal model in which colon cancer is induced by the genotoxicant AOM (Azoxymethane), E171 was able to dramatically enhance the tumour formation induced by AOM.
The intervention study that is described in this METC protocol is done in the context of a project that aims to establish the potential risk of stimulation of the development of colorectal cancer in humans due to ingestion of the food additive E171. The hypothesis for the mechanism that may explain the effect is that E171 induces inflammation in the colon, and that the inflammatory

condition would facilitate the development of colorectal cancer. The intervention study aims at measuring inflammatory and genomic markers that may be early indicators of the development of colorectal cancer. The information yielded by this study will allow to extrapolate the findings in animals concerning the facilitation of the development of colorectal cancer to humans, and perform a risk assessment. The selection of markers to be used in the intervention study will be based pervious animal and in vitro experiments.

Study objective

In this intervention study, the primary aim is to evaluate the influence of E171 exposure on the gene expression profile in rectal biopsies. In addition, inflammatory markers such as ROS in the rectal epithelium will be measured as secondary outcome.

Study design

This human volunteer study has a cross-over design with only healthy volunteers divided in 2 groups, one that will start with the control period and the other one that will start with the intervention period. Each participant will undergo proctoscopy after each study period, rectal biopsies and rectal swap will be taken. In addition, subjects will be asked to donate blood.

Intervention

During the study, the subjects will follow two different periods: a two weeks control period and a two weeks intervention period.
The aim of the control period is to reduce to a minimum the exposure to E171. Therefore, the subjects will be given a list of tiO2-containing products to avoid during these two weeks.
The aim of the intervention period is to observe the effect of E171 in the colon, by making a gene expression profile and measuring biomarkers of exposure to E171. For this, the subjects will be given yoghurt to eat 3 times a day in which a normal daily amount of E171 will be added.

Study burden and risks

The burden / risk / benefit associated with participation will be as follows:

-2 colonic biopsies (after each study period (control and intervention period)). Biopsies will be collected by proctoscopy and therefore no specific preparation is necessary. This procedure is used daily in medical practice and is a relatively safe examination method. Complications are very rare. Bleeding may occur from biopsies, but is minimal and stops quickly. If rectal bleeding persists, the volunteer must report this immediately.
-2 rectal swaps; this procedure is without any specific risk;

- 2 blood samples will be collected (one sample after each study period). The risks related to the collection of these samples are minimal;
- keeping a dietary registration.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthey volonteers with a Body Mass Index (BMI) between 18-27, male or femelle and between 18-70 years old

Exclusion criteria

- Alcohol abuse up to 6 months before participation in this research, i.e. more

than 4 drinks on any single day and more than 14 drinks per week for men and more than 3 drinks on any single day and more than 7 drinks per week for women
- Current presence of any diseases related to the gastrointestinal tract, kidney, liver, heart or lungs
- Current presence of symptoms related to diseases of the gastrointestinal tract, i.e. vomiting, diarrhoea or constipation, and altered stool, such as blood in stool
- Current presence of diseases related to the endocrine or metabolic system
- Current presence of anaemia
- HIV infection or hepatitis
- Use of antibiotics and other prescribed medication and painkillers over the last 3 months (exception: paracetamol and anti-contraceptive)
- Current smokers
- Vegetarians
- Pregnant women
- Participants of other intervention studies during this intervention period.
- Participants who use anticoagulant medicine

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-05-2019
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	05-12-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-12-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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: 20868
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL52433.068.16
Other	NTR (TC = 5880)
OMON	NL-OMON20868

Study results

Date completed: 01-04-2024

Summary results
Trial ended prematurely