Risk of intake of E171 on development of colorectal cancer

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21855

Bron
Nationaal Trial Register

Verkorte titel
E171 and colon cancer

Aandoening

Colorectal cancer

Ondersteuning

Primaire sponsor: Maastricht University
Overige ondersteuning: NVWA

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The main outcome parameter in this study is the difference in the gene expression profiles due to exposure to the food additive E171.

In order to evaluate the impact of the food additive E171 on gene expression changes and to modify molecular processes involved in human cancer development colon biopsies will be analysed for transcriptomic responses to the exposure to E171.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:
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 (TiO2) particles of various sizes, among others in the nanoparticle size range. TiO2 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 will be 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, that will include gene expression changes, to be used in the intervention study will be based on preclinical research using in vivo animal models and cell systems of human origin in vitro exposed to E171.

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 and blood will be measured as secondary outcome. Effect on the microbiome will be assessed in the rectal swaps.

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 by a specialised nurse. In addition, subjects will be asked to donate blood. Data analysis to examine effects of E171 in food will be done after the end of the study and the wash-out period serves as a control.

Study population:
All subjects will be recruited by the University of Maastricht (UM), the Netherlands, using

advertisements in local newspapers as well as other media. Healthy subjects of both sexes will be selected based on predefined inclusion criteria (BMI: 18-27; > 18 years) and randomly assigned to one of the different experimental groups.

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 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.
After each period of two weeks, colonic biopsies will be taken at the hospital of Sittard during a proctoscopic examination made by a specialised nurse. In addition, blood and rectal swaps will be sampled and stored appropriately at UM for later analysis.

Main study parameters/endpoints:
- The primary outcome parameters are differences in transcriptomic markers after consumption of food additive E171. These outcomes in humans will shed light on the relevance of markers identified in preclinical studies, and how the animal data on the risk of facilitation of tumour growth can be extrapolated to humans.
- Secondary outcome parameters include inflammatory markers such as ROS in the rectal epithelium and blood. A rectal swab will be taken in order to evaluate the effect on the microbiome. These outcomes will help to understand the inflammatory mechanisms that may be indicative of the risk to developing colorectal cancer.

Doel van het onderzoek

We hypothesize that E171 induces gene expression changes in the colon that explain the inflammatory mechanism of E171 in the colon, which facilitate the development of colorectal cancer. In addition, inflammatory markers will be increased in the rectum and blood of participants consuming standard levels of E171.

Onderzoeksopzet

Two time points: This study will be done in 4 weeks and include 2 periods. The volunteers will be randomized in two groups: one group will start with the intervention period and the other one will start with the control period. After these 2 weeks of intervention or control periods, a first test day will follow (time point 1) at which biological samples will be gathered. Next, the volunteers will start the control period and intervention period respectively for another 2 weeks. After these 2 weeks of intervention or control periods, a second test day will follow (time point 1) at which biological samples will be gathered.

Onderzoeksproduct en/of interventie

This study is a cross-over design and will be done in 4 weeks and include 2 periods. The

volunteers will be randomized in two groups: one group will start with the intervention period and the other one will start with the control period. After, these 2 weeks of intervention or control periods, the volunteers will start the control period and intervention period respectively for another 2 weeks. The control period, is meant to reduce to a minimum the ingestion of E171 in order to have all the volunteers to start the same level of E171. During this period the volunteers will receive a list of products to avoid like cookies, chewing gum, certain toothpaste that are known to contain a significant amount of E171.The intervention period, is meant to control the amount of E171 that the volunteers will ingest. A concentration, 0.82 mg/kg bw/day, corresponding to a normal daily consumption will be given to the volunteers. The quantity will be adjusted to the body weight and dispersed in yoghurt that will be eaten at breakfast, lunch and dinner.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Healthy with a Body Mass Index (BMI) between 18-27, male or female
- Between 18-70 years old

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- 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 contraceptive)
- Current smokers
- Vegetarians
- Pregnant women
- Participants of other intervention studies during this intervention period.
- Participants who use anticoagulant medicine

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-06-2020
Aantal proefpersonen:	80
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Toelichting
N.A.

Ethische beoordeling

Positief advies

Datum:	15-04-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8534
Ander register	METC azM/UM : METC 163010

Resultaten

Samenvatting resultaten
No publications yet