The effect of polyethylene glycol treatment on gut health in Cystic Fibrosis, a pilot study

Published: 08-08-2019
Last updated: 09-04-2024

Main objective: to assess the effects of PEG treatment on bile acid homeostasis in cystic fibrosis patients. Secondary objective: to assess the effects of PEG treatment on gastrointestinal symptoms and quality of life, and on gut health-related...

Ethical review	Approved WMO
Status	Pending
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON48606

Source
ToetsingOnline

Brief title
Polyethylene glycol treatment in cystic fibrosis

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Exocrine pancreas conditions
- Respiratory tract infections

Synonym
Cystic Fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Nederlandse Cystic Fibrosis Stichting

Intervention

Keyword: Bile acid metabolism, Cystic Fibrosis, Gut health, Polyethylene glycol

Outcome measures

Primary outcome

change in plasma levels of fibroblast growth factor 19 (FGF19) after 2 weeks of laxative treatment.

Secondary outcome

- Changes in subjective parameters related to intestinal health as measured by the corresponding sections of the validated the cystic fibrosis questionnaire (CF-Q), namely gastrointestinal complaints, general wellbeing/condition and treatment burden.

- Changes in objective parameters related to intestinal health, among which different metabolic processes:

Plasma parameters:

o Bile acid metabolism: C4, bile acid profile

o Glucose metabolism: (fasted) Glucose, HbA1c, insulin

o Liver function: GGT, ASAT, ALAT, thrombocytes, albumin

o Cholesterol metabolism: lipoprotein profile, triglycerides

o Gut health: glucagon-like peptide 1, serotonin (5-HT)

- Faecal parameters:

o Microbiota composition

o Inflammation: calprotectin, lactoferrin, IgA

o Elastase

o Neutral sterols

Study description

Background summary

Gut health in cystic fibrosis (CF) is impaired. The CF gastrointestinal phenotype is characterized by nutrient malabsorption, dysbiosis and intestinal inflammation. The prominent role of the gut in numerous metabolic processes and its influence on other organs has recently become well appreciated. Impaired gut health in CF is likely to play a important role in CF-related liver disease as well as metabolic complications such as CF-related diabetes mellitus. Impaired gut health in CF is also associated with bothersome symptoms as abdominal discomfort and constipation.
In this study, we aim to evaluate the effects of treatment with polyethylene glycol (PEG), a commonly prescribed osmotic laxative , on gut health in CF patients by both clinical symptoms and biochemical parameters. In animal models of CF, we have recently shown that PEG treatment improves various gastrointestinal outcomes, among which bile acid homeostasis, which could be implicated in the pathophysiology of CF-related complications such as diabetes and liver disease. In addition, others reported that PEG improves intestinal transit time and reduce small intestinal bacterial overgrowth in CF mice; thus, by improving gut function, short-term benefits on gastrointestinal symptoms and general wellbeing are also expected.
Measurements, including both blood and faecal parameters related to gut health and a quality of life questionnaire, will be collected from CF patients before, 2 weeks after PEG treatment, and after a 2-weeks washout period.
If PEG treatment improves gut health according to the measured parameters, as it does in animal models, it should be considered as a possible treatment to improve gut health in CF patients.

Study objective

Main objective: to assess the effects of PEG treatment on bile acid homeostasis in cystic fibrosis patients. Secondary objective: to assess the effects of PEG treatment on gastrointestinal symptoms and quality of life, and on gut health-related parameters, such as liver function and glucose metabolism.

Study design

Longitudinal repeated measures design. Measurements will be at baseline (day 0), after 2 weeks of PEG treatment (day 14) and after 2 weeks of wash-out

period (day 28). Each measurement consists of taking blood, filling a questionnaire and collect faeces.

Intervention

Polyethylene glycol + electrolytes (Movicolon) 13.8 gram twice daily for 2 weeks

Study burden and risks

Intestinal health in CF is impaired, with consequently many possible complications on gastrointestinal and metabolic processes. With promising results of PEG in animal studies in improving gut health and mostly bile acid homeostasis, this study will gain insight in the therapeutic opportunities in humans. This can have a contribution to the future treatment of CF patients. The burden for participants will be acceptable. Patients will be asked to visit the hospital three times for a fasted blood draw and questionnaire. Additionally, patients will be asked to collect three faecal samples. We expect no pressing adverse events. Patients are treated with a commonly prescribed laxative for a period of two weeks. The most common side effects associated with PEG use are: diarrhea, which might occur in absence of overt constipation, abdominal distention, stomach pain, stomach cramps, nausea, vomiting, flatulence, borborygmi. More serious complications as electrolyte disturbances and allergic reactions are rare. Expected benefit in improvement gastrointestinal and subjective well-being, especially on the long-term, is potentially significant.

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

- Cystic fibrosis confirmed by genetic analysis
- Exocrine pancreatic insufficiency as reflected by the use of prescribed pancreatic enzyme replacement therapy (usually Creon).
- Age of 18 years or above at the time of enrollment in the study

Exclusion criteria

- A current therapeutic antibiotic course for pulmonary exacerbation or need for hospitalization for antibiotic treatment (does not include prophylactic long-term antibiotic use)
- Standard prescribed daily treatment with any laxative at the moment of inclusion, because it will be undesirable to stop treatment during the washout period. Occasional treatment with laxatives is not an exclusion criteria.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2019
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Movicol
Generic name:	Macrogol 3350/elektrolytes
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	08-08-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2017-002520-24-NL

Register	ID
CCMO	NL66236.042.19