The effect of riboflavin supplementation on Faecalibacterium prausnitzii in Crohn's disease

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The present study will evaluate if supplementation of the diet with riboflavin in Crohn*s disease patients will result in a similar increase in the number of F. prausnitzii as seen in the healthy volunteers. Potentially an even larger effect can...

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

Summary

ID

NL-OMON41902

Source
ToetsingOnline

Brief title
Riboflavin in Crohn's disease / RISE-UP study

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
Crohn's disease, M. Crohn

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Bacterial composition, M. Crohn, Riboflavin, Vitamin B2

Outcome measures

Primary outcome

1). To investigate the effect of a riboflavin supplement on the number of F. prausnitzii bacteria in the faeces of active and quiescent Crohn*s disease patients.

Secondary outcome

1). To evaluate the effect of a riboflavin supplement on the bacterial composition in the faeces of active and quiescent Crohn*s disease patients.

2). To evaluate the effect of a riboflavin supplement on the production of short chain fatty acids (SCFAs) in the faeces of active and quiescent Crohn*s disease patients.

3). To assess the effect of the riboflavin intervention on the disease severity (Harvey Bradshaw Index, IBD-Q and faeces Calprotectin) of active and quiescent Crohn*s disease patients.

4). To evaluate the effect of the riboflavin intervention on permeability of the gut in active and quiescent Crohn*s disease patients (Chroom-EDTA test, and different biomarkers of permeability).

5). To determine the effect of a riboflavin supplement on the faecal pH in active and quiescent Crohn*s disease patients.

6). To evaluate whether riboflavin intervention leads to an increase in electrical current, as a result of an increase in extracellular electron

shuttling bacteria.

Study description

Background summary

Recent studies show that in patients with inflammatory bowel disease (IBD) a dysbiosis exists in the composition of the intestinal microbiota. In particular, the potentially pathogenic bacterium Escherichia coli (E. coli) is often more abundant in the bowel of IBD patients, and the anaerobic commensal Faecalibacterium prausnitzii (F. prausnitzii) is often reduced. This last mentioned bacteria is known to be abundant in the intestine of healthy individuals. It is known to produce butyrate, which stimulates the intestinal epithelium, and to secrete anti-inflammatory substances.

Riboflavin - also known as vitamin B2 - is required for a wide variety of cellular processes and has an important role in maintaining health in humans. In a pilot intervention with healthy volunteers it is shown that a riboflavin supplement increases the number of F. prausnitzii and results in a higher production of butyrate. In Crohn*s disease patients, it is known that the amount of F. prausnitzii in the intestine is generally low. Furthermore, it is known that there is an association between the number of F. prausnitzii bacteria and the length of disease in remission.

This study will evaluate if supplementation of the diet with riboflavin in Crohn*s disease patients will result in a similar increase in the amount of F. prausnitzii as in healthy volunteers. In this patient group, an increase in the number of F. prausnitzii bacteria in the bowel may result in a more favourable disease course. This will be assessed with faeces calprotectin and two questionnaires. Additionally we will assess if there is any modulation by riboflavin on the other intestinal bacteria, short chain fatty acids (SCFAs) (such as butyrate), and the pH of the faeces. Finally, the effect of the riboflavin on the permeability of the gut will be evaluated with a Chroom-EDTA test, and a number of different biomarkers of permeability.

The hypothesis is that in Crohn*s disease patients, supplementation of the diet with riboflavin results in an increase in the amount of F. prausnitzii, changes in microbial composition, increased fatty acid production, an increase in pH and a reduction of intestinal permeability. These changes might result in a more favourable disease course with less exacerbations.

Study objective

The present study will evaluate if supplementation of the diet with riboflavin

in Crohn*s disease patients will result in a similar increase in the number of F. prausnitzii as seen in the healthy volunteers. Potentially an even larger effect can occur, because of the low starting amount. In this patient group, an increase in the number of F. prausnitzii may result in a more favourable disease course.

Study design

Prospective clinical study.

Intervention

Supplementation of the normal diet with 1 capsule (100 mg) of riboflavin (vitamin B2) during three weeks.

Study burden and risks

Participating in this study has a potential health benefit. It is known that in healthy subjects, the supplement riboflavin increases the amount of beneficial bacteria. In Crohn*s disease there is often a dysbiosis of the bacterial composition, and the beneficial bacteria are depleted. When a similar increase in the beneficial bacteria occurs in Crohn*s disease patients as seen in healthy volunteers, this may result in a more favourable disease outcome (staying in remission longer). Riboflavin is freely available, and commonly sold in health shops. There is no need for a prescription to buy this supplement, and its use is considered to be safe. The riboflavin supplement may give a (completely innocent) yellow discoloration of the urine several hours after ingestion. There is no need to discontinue the riboflavin supplementation. The adverse event of discoloration of urine is only temporary.

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

Group 1 (n=42)
- Patients diagnosed with Crohn*s Disease in remission (Calprotectin < 200 µg/g)
- Age 18-65 years;Group 2 (n=42)
- Patients diagnosed with Crohn*s Disease with active disease (Calprotectin > 200 µg/g)
- Age 18-65 years

Exclusion criteria

- Swallowing disorders
- Pregnancy and lactation
- Use of antibiotic drugs, probiotics (i.e.Yakult, Vifit, Activia etc) or specific prebiotic supplements in the 3 weeks prior to the riboflavin intervention (for a list of probiotic, prebiotic and other supplements see attachment 2)
- Use of Methotrexate drugs.
- Colonoscopy and colon cleansing in last 3 months
- Use of a vitamin B2 supplement, or multivitamin complexes containing vitamin B (i.e. vitamin B-complex) in the 3 weeks prior to the riboflavin intervention
- Severe Crohn*s disease (HBI > 12)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-01-2016
Enrollment:	84
Type:	Actual

Ethics review

Approved WMO Date:	20-04-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-03-2016
Application type:	Amendment
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
Other	Het onderzoek wordt na goedkeuring geregistreerd op clinicaltrials.gov.
CCMO	NL48186.042.14