Applying Manuka Honey in Gastroenterology

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Ethical review	Not approved
Status	Will not start
Health condition type	Gastrointestinal infections
Study type	Interventional

Summary

ID

NL-OMON45863

Source
ToetsingOnline

Brief title
Manuka and GI disorders

Condition

- Gastrointestinal infections
- Bacterial infectious disorders

Synonym
Diarrhea

Research involving
Human

Sponsors and support

Primary sponsor: TweeSteden ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: antibacterial, ant-inflammatory, bacteriostatic, clostridium difficile, gastroenterology, honey, irritable bowel syndrome, Manuka, microscopic colitis

Outcome measures

Primary outcome

Primary outcome measure:

- Frequency of stools

- Consistency of stool as measured using the Bristol Stool Scale

Secondary outcome

Secondary outcome measures

- Recurrence of abdominal symptoms after start intervention measured using the

Gastro-intestinal Symptom Rating Scale (GSRS)

- Recurrance of symptoms attributed to irritable bowel disorder measured using

the Birmingham IBS symptom questionnaire

- Quality of life (QOL) measured using the Ferrans and Powers QOL-Index

Study description

Background summary

Honey is a substance with a long tradition of use in medicine going back to ancient Egypt. Research shows wide therapeutic potential, demonstrating An anti-oxidant, bacteriostatic, andt-inflammatory and antimicrobrial properties. It is a carbodydrate rich syrope produced by bees, primarliy from floral nectars. The major components are fructose and glucose, however a large number of other chemical components are present in small amounts, varying depending on the type of honey.

The therapeutic mechanism of honey has not yet been fully elucidated. However, an antibacterial effect has been attributed to osmolarity, hydrogen peroxide generation and unidentified additional phytochemical components3. Furthermore,

as well as antibacterial activity, honey has been shown to have an anti-inflammatory function5. The anti-inflammatory effects may be due to antioxidant components.

Numerous studies have demonstrated that unprocessed honeys have antibacterial activity against a range of pathogens. The investigated pathogens include isolates of diarrhoea causing bacteria, isolates from infected community, nosocomial wounds and burns, bacterial infections of the conjunctiva and other ocular surface diseases. Our research team1, as well as other clinical researchers2 have performed in vitro studies demonstrating that unprocessed honeys have antibacterial activity against a range of pathogens, including Clostridium difficile.

Clostridium difficile (CD) associated disease is an increasingly common health problem. C. difficile is a causative agent of antibiotic associated pseudomembranous colitis, antibiotic associated colitis and antibiotic associated diarrhea4. CD overgrowth usually occurs during antibiotic therapy, as the normal gastrointestinal flora is disrupted. Discontinuation of antibiotics does not lead to symptomatic improvement and new strains of the pathogen have a substantial failure rate after therapy cessation5.

Microscopic colitis (MC) is an umbrella term for chronic watery diarrhea with a normal macroscopic appearance of the colonic mucosa by endoscopy though with typical histological inflammatory changes. MC includes two main subtypes, i.e. collagenous colitis (CC) and lymphocytic colitis (LC). Over 80% of MC patients respond well on induction therapy with oral budesonide6. However, approximately 60-80% of all patients experience symptom relapse after cessation of treatment (after 3-6 months) and require additional low dose budesonide maintenance therapy7,8,9. A considerable proportion of the relapsing patients (10-20%) will finally turn out to be non-responder to oral budesonide9. Risk-factors for primary non-response are unknown. Unfortunately, an alternative evidence based treatment is not yet available. The exact pathophysiological mechanisms of chronic diarrhea in MC are not clarified. A clear association between MC and concomitant autoimmune disorders like rheumatic disease, celiac disease and thyroid disease is described10,11, suggesting MC to be an auto-immune mediated disorder. Furthermore, drug-induced inflammation, bile-salt malabsorption and changes in the epithelial barrier function (e.g. increased permeability) due to luminal factors12 are considered as contributing factors to MC development. However, the exact mechanisms remain to be elucidated.

Functional gastro-intestinal disorders (FGID) are common disorders which present with persistent and recurring GI symptoms. More than 20 FGID have been identified, the most commonly known being Irritable Bowel Syndrome (IBS)13. FGID are thought to have a multifactorial pathophysiology including gastro-intestinal (GI) infections, dietary intake, and stress may all play a role in disease development. No golden standard exists for treatment of IBS. Treatment decisions are often based on severity of symptoms and the

relationship of IBS with possible influential factors such as diet, or psychosocial comorbidities. The current consensus is that milder symptoms are primarily related to visceral hypersensitivity and treatment therefore constitutes pharmacology targeting the GI tract itself14. More severe symptoms are generally correlated to psychosocial difficulties and treatment often requires the use of antidepressant medications or psychological treatment14.

Study objective

The aim of this study is to investigate efficacy of a manuka honey lavage in the treatment of three distinct disorders; persistent clostridium difficile infection (CD), budesonide dependent microscopic colitis (MC), and therapy refractory irritable bowel syndrome patients with the diarrhea subtype (IBS-D).

Study design

We propose a single center RCT in which 3 groups of patients who have been deemed therapy refractory will undergo treatment with a colonic lavage using Manuka honey. These groups will be compared to a placebo group within each diagnostic criteria. These three patient groups consist of:
1. Patients with a persistent clostridium difficile infection who either do not respond to antibiotic therapy or do not tolerate antibiotics
2. Patients with diagnosed microscopic colitis who have received maximum budesonide treatment, and experience relapse of symptoms during step-down dosages, defined as budesonide dependent patient*s
3. Patients diagnose with irritable bowel syndrome patients of diarrhea subtype according to the Rome IV criteria, whose symptoms persist despite 6 months of treatment via the outpatient clinic

All patients who fulfill the inclusion and exclusion criteria will be asked for inclusion via the gastroenterology outpatient clinic. Upon inclusion, patients will be entered into an anonymous database, only accessible to the primary researcher at each intervention site.

Following inclusion and informed consent a planned colonoscopy will take place. This will occur according to standard procedure at each intervention site. At the time of colonoscopy a colonic lavage will be performed. A dilution of 20% manuka honey (MGO 550+) in a quantity of 250 ml will be sprayed through a specialized nozzle attached to the endoscope, and will be distributed throughout the entire colon starting at the cecum.

Following colonoscopy a patient will be discharged and will receive follow up check-ups at 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks and 1 year. At each of these follow-up momentsthe following outcome measures will be gathered: the GSRS, Birmingham IBS questionnaire, Quality of Life (QOL) Index and specifics

regarding frequency and consistency of stool according to the Bristol Stool Scale.

Successful treatment will be defined as a stool frequency less than 3 times daily and a consistency of 4 or less according to the Bristol stool scale.

In the case of microscopic colitis patients receiving treatment with budesonide, following successful treatment at week 2 follow-up, all patients will be asked to slowly decrease dosages of budesonide and resume the follow-up period, with instructions to contact the primary researcher should symptoms reoccur. If symptoms reoccur this will be defined as failure of therapy, and the original therapy with budesonide will resume.

Intervention

Following inclusion and informed consent a planned colonoscopy will take place. This will occur according to standard procedure at each intervention site. At the time of colonoscopy a colonic lavage will be performed. A dilution of 20% manuka honey (MGO 550+) in a quantity of 250 ml will be sprayed through a specialized nozzle attached to the endoscope, and will be distributed throughout the entire colon starting at the cecum.

Study burden and risks

The burden and risks associated with participation are conform the risks of a colonoscopy. These risks include bleeding, perforation of the bowel, and adverse reactions to the sedation. These risks are limited by not performing any biopsies during colonoscopy within the parameters of this trial.

The patients to be included in the trial are therapy refractory. This means that they suffer from severe gastrointestinal symptoms, with the chief complaint being diarrhea, often having a severe impact on their quality of life. No treatments in the standard care are sufficient to aid in symptom relief. The possibility of this experimental treatment doing so, and the possible improvement in quality of life justifies the risks and burdens associated with participation in this trial.

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

All patients seen at the outpatient clinic in either Elisabeth-TweeSteden Hospital in Tilburg, or the Maastricht University Medical Center with any of the following diagnoses will be eligible for inclusion: ;1. Patients with a persistent clostridium difficile infection who either do not respond to antibiotic therapy or do not tolerate antibiotics;2. Patients with diagnosed microscopic colitis who have received maximum budesonide treatment, and experience relapse of symptoms during step-down dosages, defined as budesonide dependent microscopic colitis ;3. Patients diagnose with irritable bowel syndrome patients of diarrhea subtype according to the Rome IV criteria, whose symptoms persist despite 6 months of treatment via the outpatient clinic ;- Therapy refractory defined as patients with a definitive diagnosis who continue to have a defecation frequency above 3 times daily, with at least one of these times a consistency of 5 or 6 according to the Bristol Stool Scale. ;- A minimum of 1 year follow up;- Age older than 18 years old at diagnosis

Exclusion criteria

- Patients younger than 18 years of age ;- Comorbidities of gastro-intestinal tract;- Drug or alcohol abuse

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	60
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	MGO 550+ Manuka Honey
Generic name:	MGO 550+ Manuka Honey
Registration:	Yes - NL outside intended use

Ethics review

Not approved

Date:	10-04-2017
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

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	EUCTR2017-001358-33-NL
CCMO	NL61459.028.17