Donor feces infusion for first episode of Clostridium difficile infection in patients at risk for recurrent infection

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The primary objective of this study is to investigate whether FMT after antibiotic therapy is more effective than conventionalantibiotic therapy alone in patients with a first episode of CDI.

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

Summary

ID

NL-OMON43385

Source
ToetsingOnline

Brief title
FMT first episode CDI

Condition

- Gastrointestinal infections
- Bacterial infectious disorders

Synonym
Clostridium difficile infection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: CDI, Clostridium difficile infection, Fecal microbiota transplantation, FMT, High risk recurrent CDI

Outcome measures

Primary outcome

Primary endpoint is cure (no diarrhea) without relapse. Cure is defined as absence of diarrhea; or normalization of the stool pattern with a negative C. difficile test in patients with pre-existent frequent bowel movements. Relapse is defined as a new episode of diarrhea confirmed by a positive stool C. difficile within 10 weeks after the initiation of therapy.

Secondary outcome

It is largely unknown which factors contribute to treatment efficacy. The composition of the microbiota may play an important role. We will analyze the microbiota of patients before and after treatment and will apply metagenomics to determine which bacterial species are essential for protection against CDI.

The economic evaluation focuses on the cost-effectiveness and cost-utility of FMT and vancomycin with a 6-month time horizon. The analysis will be performed from a societal perspective based on the incremental costs per decrease of CDI recurrence.

Study description

Background summary

Clostridium difficile is the most common cause of antibiotic-associated diarrhea. Because of more virulent strains and evolving antimicrobial resistance, incidence, outbreaks, mortality, and recurrent CDI have increased in the past decade.
Unfortunately, about 25% of patients with CDI experience recurrent disease; this proportion rises to 70% in patients with multiple recurrences. The most important cause of recurrent CDI is persistent disruption of the intestinal microbiota. Patients with recurrent CDI can be cured with FMT (defined as the transfer of intestinal microbiota from a healthy donor), which restores the healthy microbiota. Using a clinical prediction rule, patients at risk (>35%) for recurrent CDI can be identified.
To date, studies on FMT have focused on treatment of recurrent CDI. The aim of our study is to investigate the potential benefit of FMT after antibiotic treatment to prevent all recurrences of CDI in patients at high risk (35%-45%) of treatment failure.
Prevention of recurrent CDI is the most effective way to reduce morbidity, mortality and health care costs.

Recently the Netherlands National Donor Feces Bank (NNDFB) was founded to facilitate FMT and to standardize the protocol, which will lead to cheaper, safer and wider availability of this new treatment approach. The NNDFB aims to provide hospitals with screened, frozen material ready for clinical use. We propose to investigate the use of FMT with frozen suspensions provided by the NNDFB as treatment of a first episode of CDI in a randomized controlled trial.

Study objective

The primary objective of this study is to investigate whether FMT after antibiotic therapy is more effective than conventional antibiotic therapy alone in patients with a first episode of CDI.

Study design

Our study is designed as a monocenter, open label, randomized trial comparing donor feces infusion (223 ml) preceded by 10 days vancomycin (250 mg q.i.d.) and bowel lavage (1 liters Moviprep® or 2 liters KleanPrep®) to 10 days of vancomycin (250 mg orally q.i.d.). Patients will be randomly allocated at 1:1 ratio to the two treatment options.

Intervention

Duodenal infusion of donor feces (provided by the NNDFB), after a 10-day course of vancomycin (250 mg orally q.i.d.) with
bowel lavage one day prior to FMT.

Study burden and risks

Full colon lavage and insertion of nasoduodenal tube could cause inconveniency. Studies which evaluated donor feces infusion against recurrent CDI reported no serious adverse events directly related to donor feces infusion. Main side effects of donor feces infusion are diarrhea, cramping, belching, nausea, abdominal pain, and dizziness, which resolve within a few days.
Participating patients are asked to collect fecal samples before and after FMT. Patients will have brief scheduled telephone contacts at 1 week, 2 weeks, 4 weeks, and 6 weeks after FMT to discuss recovery and presence of recurrence or adverse events.

Overall success rate of donor feces infusion against CDI has been proven to be 90%. However, no data is available with regard to an initial episode of CDI.
The biggest benefits of donor feces infusion are restoring the gut microbiota and the possibility of eradication of C. difficile without exposure to antibiotics. The use of antibiotics like vancomycin does not restore the gut microbiota. Long term effects of FMT are still unknown.

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

Microbiologically confirmed first episode of Clostridium difficile infection
> 17 years
Risk estimation score >2 by using the prediction model of D'Agostino Sr et al.
Patients should be able to give informed consent

Exclusion criteria

Use of antibiotics other than for CDI at the day of inclusion
Pregnancy
Dysphagia

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2016
Enrollment:	158
Type:	Actual

Ethics review

Approved WMO

Date:	22-02-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
CCMO	NL55646.029.15