¡®Faecal microbiota transfusion for decolonization of multidrug resistant Enterobacteriaceae in renal transplant recipients (RESET): a pilot study.¡¯

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Renal transplant patients are at increased risk of colonization and infection with multidrug resistant Enterobacteriaceae (MDRE) due to medications that modify their immune systems, increased healthcare and antibiotic exposure, and surgical...

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22882

Bron
NTR

Verkorte titel
RESET

Aandoening

multi drug resistance colonization
renal transplant recipients
MDR infections
faecal microbiota transfusion

Ondersteuning

Primaire sponsor: Department of Infectious Diseases and Medical Microbiology, Leiden

University Medical Center
Overige ondersteuning: Vedanta Biosciences, Inc.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Frequency and magnitude of any adverse events within 1 month of faecal microbiota transfusion, including infections. The occurrence of renal transplant related adverse events (graft loss, biopsy-proven acute rejection, doubling of serum creatinine) within 3 months after FMT.

Toelichting onderzoek

Achtergrond van het onderzoek

SUMMARY

Rationale: Renal transplant patients are at increased risk of colonization and infection with multidrug resistant Enterobacteriaceae (MDRE) due to medications that modify their immune systems, increased healthcare and antibiotic exposure, and surgical alteration of the urinary tract [Pinheiro 2010]. Innovative strategies for decolonization of MDR bacteria are urgently needed to reduce hospital admissions, the use of reserve antibiotics and to prevent transmission. Currently, effective decolonization strategies are lacking and targeted selective digestive decontamination seems to result in short term benefits only. Successful eradication of intestinal MDRE colonization by faecal microbiota transfer (FMT) has been reported in immunocompetent patients [Manges 2016, Davido 2017, Singh R et al, 2014]. FMT appears to be safe and effective in immunocompromised patients with recurrent Clostridium difficile infections [van Nood 2013, van Beurden 2016, Kelly 2014] and is a potential eradication treatment for renal transplant recipients with intestinal MDRE colonization.

Objective: To assess the safety and efficacy of faecal microbiota transfusion to eradicate intestinal colonization with MDRE in renal transplant patients with a history of infection caused by these MDR bacteria. Targeted bacteria are extended-spectrum β-lactamase Enterobacteriaceae (ESBL-E) and carbapenemase producing Enterobacteriaceae (CPE).

Study design: Interventional pilot study, 1:1 randomized controlled trial with 12 participants, follow up of 6 months.

Study population: Consenting adult female renal transplant recipients (≥18 years), with intestinal carriage of one of the target MDR organisms by rectal swab or stool culture tests

(at least on two occasions), and a history of at least one documented infection by these bacteria within 6 months before enrolment.

Exclusion criteria: need for systemic antibiotics at enrolment; ICU admission at enrolment; creatinine clearance <30 ml/min; (planned) pregnancy during study duration; allergy or other contraindication to one of the study drugs; recurrent aspirations / chronic dysphagia; recent intra-abdominal surgery; recent treatment with alemtuzumab or eculizumab; active colitis / gastro-enteritis or inflammatory bowel disease; severe food allergy.

Intervention:

Intervention group (6 subjects): Oral gut decontamination regimen colistin sulphate (1.000.000 E 4×/day) and neomycin sulphate (250 mg 4×/day) for 5 days, combined with nitrofurantoin (100 mg 2×/day) for 5 days if MDRE bacteriuria is present, followed by bowel lavage on day 6. Patients will receive Omeprazole 20 mg per os 1 dose on the evening of day 6 and on the morning of day 7. On day 7 200 ml of standardized faecal suspension will be infused through a nasoduodenal tube. FMT will be matched with regard to donor / recipient cytomegalovirus and Epstein-Barr virus serology.

Control group (6 subjects): Oral decontamination regimen for 5 days as described above.

Main study parameters/endpoints:

Primary study parameters:

Frequency and magnitude of any adverse events within 1 month of faecal microbiota transfusion, including infections. The occurrence of renal transplant related adverse events (graft loss, biopsy-proven acute rejection, doubling of serum creatinine) within 3 months after FMT.

Secondary / exploratory study parameters:

- Number of participants with intestinal carriage of MDRE after FMT (assessed at 1 and 2 weeks and 1, 3 and 6 months after FMT).

- Number of participants with one or more MDRE infection(s) within 6 months after FMT.

- Change (relative to baseline) in the microbiota composition during 6 months of follow-up.

- Change in microbiome diversity, calculated by Shannon diversity index, during 6 months of follow-up.

- Prevalence of antibiotic resistance genes in faecal samples during 6 months of follow up as determined by metagenomics.

- Magnitude of intra-patient variability in immunosuppressive drug exposure.

Doel van het onderzoek

Renal transplant patients are at increased risk of colonization and infection with multidrug resistant Enterobacteriaceae (MDRE) due to medications that modify their immune systems, increased healthcare and antibiotic exposure, and surgical alteration of the urinary tract. Innovative strategies for decolonization of MDR bacteria are urgently needed to reduce hospital admissions, the use of reserve antibiotics and to prevent transmission. Currently, effective decolonization strategies are lacking and targeted selective digestive decontamination seems to result in short term benefits only. Successful eradication of intestinal MDRE colonization by faecal microbiota transfer (FMT) has been reported in immunocompetent patients. FMT appears to be safe and effective in immunocompromised patients with recurrent Clostridium difficile infections and is a potential eradication treatment for renal transplant recipients with intestinal MDRE colonization.

Onderzoeksopzet

Screening visit

Intervention period with 5 days of SDD (with or without FMT)

Follow up 1,2,4,12 and 24 weeks after the intervention

Onderzoeksproduct en/of interventie

Intervention:

Intervention group (6 subjects): Oral gut decontamination regimen colistin sulphate (1.000.000 E 4¡Á/day) and neomycin sulphate (250 mg 4¡Á/day) for 5 days, combined with nitrofurantoin (100 mg 2¡Á/day) for 5 days if MDRE bacteriuria is present, followed by bowel Version 1.0, 14-06-2017 9 of 45 lavage on day 6. Patients will receive Omeprazole 20 mg per os 1 dose on the evening of day 6 and on the morning of day 7. On day 7 200 ml of standardized faecal suspension will be infused through a nasoduodenal tube. FMT will be matched with regard to donor / recipient cytomegalovirus and Epstein-Barr virus serology.

Control group (6 subjects): Oral decontamination regimen for 5 days as described above.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. Competent female renal transplant recipient aged 18 or above.

2. Intestinal carriage of extended-spectrum ¦Â-lactamase Enterobacteriaceae (ESBL-E) and/or carbapenemase producing Enterobacteriaceae (CPE) by rectal swab or stool culture tests (¡Ý2x).

3. A history of ¡Ý 1 documented infection by these bacteria <6 months before enrolment.

4. Adequate understanding of the procedures of the study and agrees to abide strictly thereby.

5. Ability to communicate well with the investigators and availability attend all study visits.

6. Signed informed consent.

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:

1. Need for systemic antibiotics.

2. ICU admission at enrolment.

3. Creatinine clearance <30 ml/min.

4. (Planned) pregnancy during study.

5. Allergy / contraindication study drugs.

6. Recurrent aspirations / chronic dysphagia.

7. Recent intra-abdominal surgery.

8. A history of acute rejection within 6 months before enrolment.

9. Treatment with alemtuzumab within 6 months before enrolment.

10. Treatment with of eculizumab within 3 months before enrolment.

11. Clinical signs of active colitis / gastro-enteritis, including active infections (EBV /CMV / adenovirus / Clostridium difficile / chronic parasitic infection) or active inflammatory bowel disease.

12. Severe food allergy.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland
Status: Werving nog niet gestart

(Verwachte) startdatum:	01-11-2017
Aantal proefpersonen:	12
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

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	NL6013
NTR-old	NTR6777
Ander register	METC van het LUMC : P17.167

Resultaten