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Short Report

Is faecal microbiota transplantation an option to eradicate highly drug-resistant enteric bacteria carriage?

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SUMMARY

Carbapenem-resistant Enterobacteriaceae (CRE) or vancomycin-resistant enterococci (VRE) carriage present a major public health challenge. Decolonization strategies are lacking. We aimed to evaluate the impact of faecal microbiota transplantation (FMT) on a cohort of patients with digestive tract colonization by CRE or VRE. Eight patients were included: six carrying CRE and two colonized by VRE. One month after FMT, two patients were free from CRE carriage, and another patient was free from VRE after three months. In our experience, this strategy is safe.

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Introduction

A rapid emergence of highly drug-resistant enteric bacteria (HDREB), i.e. carbapenem-resistant Enterobacteriaceae (CRE) and vancomycin-resistant enterococci (VRE), is occurring worldwide.[1] Patients carrying these bacteria are at risk of developing severe infections due to these bacteria; these infections are associated with a high mortality rate, partially because of inappropriate antimicrobial treatment.[2,3]

The use of transmission precautions such as contact isolation with patients known to be colonized or infected with resistant micro-organisms is recommended in healthcare facilities.[4] However, various adverse effects of isolation can occur in hospitalized patients, in particular a negative impact on patient mental well-being and behaviour, including higher scores for depression, anxiety, and anger.[5] A recent study also found that healthcare workers spent less time with patients in isolation.[5] Moreover, cohorting of CRE carriers often leads to a disorganization of health structure due to the necessity to have dedicated healthcare staff and area. It contributes to important direct and indirect costs.

Currently, decolonization strategies are lacking. Indeed, targeted selective digestive decontamination (SDD) for patients colonized with multidrug-resistant Gram-negative bacteria (MDRGNB) seems to result in short-term benefits only, with associated risks of resistance development to the antibiotics used.[6]

Faecal microbiota transplant (FMT) is an efficient and accepted therapy to prevent recurrent *Clostridium difficile* infection.[7] Lagier *et al*. described the first case of a patient with asymptomatic stool carriage of an OXA-48 carbapenemase-producing *Klebsiella pneumoniae* (KP) who was treated with oral colistin and gentamicin for 24 h, and then received FMT. Stool cultures and polymerase chain reaction (PCR) assays of faecal samples remained negative for KP OXA-48 7 and 14 days after the FMT procedure.[8] Millan *et al*. treated 20 patients by FMT for recurrent *C. difficile* infection, while concurrently performing a metagenomic analysis on their faeces to search for a wide range of antibiotic resistance genes before and after the procedure.[9] They found that FMT was associated with an elimination of these antibiotic resistance genes.

We identified seven different case reports of FMT being used for intestinal decolonization from extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, VRE, or meticillin-resistant *Staphylococcus aureus*.[10] In these case reports, the bacteria involved and decolonization strategies were heterogeneous. However, to the best of our knowledge, there have been no reported case series of FMT for CRE or VRE carriers. We aimed to study the impact and safety of FMT on decolonization of CRE or VRE carriers using a standardized protocol.

Methods

Setting

This was a pilot prospective multicentre study of FMT for patients with digestive tract colonization with CRE or VRE. The main outcome measure was time to successful decolonization following FMT, determined by at least two consecutive negative rectal swabs at one week interval during a three-month follow-up period.

Ethics

This study was approved by The French National Agency for Medicines and Health Products Safety (ANSM; authorization no. 140990A-41), and the French Committee of Protection of Persons (CPP; authorization no. 14064). This trial was registered under EudraCT no. 2014-003048-11. The study was conducted in accordance with the Declaration of Helsinki and the international Good Clinical Practices. Written informed consent for participation in this study was obtained from all patients.

Microbiological methods

CRE or VRE colonization was confirmed by rectal swabs. Each swab was cultured on specific selective media (chromID VRE and chromID CARBA SMART by bioMérieux®, Marcy l'Etoile, France), and on regular multidrug-resistant organism agar plates. Moreover, at admission, prior to FMT, colonization was confirmed by PCR testing (PCR Xpert CarbaR and Xpert VanA/VanB by Cepheid®, Maurens-Scopont, France).

Patients

Inclusion criteria were: aged ≥18 years; written informed consent signed; CRE or VRE colonization confirmed by at least three consecutive positive rectal swabs at weekly intervals, including one in the week prior to the FMT.

Main exclusion criteria were: immunosuppression (HIV with CD4 <200/mm^3, immunosuppressive therapy (including corticosteroids >60 mg/day for more than five days, chemotherapy); concomitant antibiotic prescription at the time of FMT.

Study procedure

During the two days prior to the FMT, patients received a proton-pump inhibitor (at the lowest dose, i.e. esomeprazole 20 mg/day). No antibiotics were administered prior to the FMT. On the day before the FMT, a naso-duodenal tube was inserted in order to perform a bowel lavage with Xprep solution.

FMT was performed using frozen preparation of faecal microbiota from a unique universal donor previously screened for potential diseases.[11] Five syringes of 50 cc of faeces diluted with saline solution were administered (1–5 mL of saline per gram of faeces).

Outcome measures

All patients had control swabs (PCR + culture) on days 7, 14, 21, and 28, and each month during three months following FMT.

Statistical analysis

Results are described as *N* (%) or median with interquartile range (IQR). Statistical analyses were carried out by GraphPad Prism v.6.0d (GraphPad Software Inc., La Jolla, CA, USA).