

Self-Administered Home Series Fecal “Minitransplants” for Recurrent *Clostridium difficile* Infection on a Rectal Remnant

Daniel Popa^{1,2}, Mihaela Laszlo³, Lidia Ciobanu^{3,4}, Elena Ucenic², Manuela Mihalache¹, Oliviu Pascu^{3,4}

1) Lucian Blaga University,
2) Polissano Clinic, Sibiu;
3) Department of
Gastroenterology, Prof. Dr.
Octavian Fodor Regional
Institute of Gastroenterology
and Hepatology;
4) 3rd Medical Clinic, Iuliu
Hatieganu University of
Medicine and Pharmacy,
Cluj-Napoca,
Romania

ABSTRACT

A fecal microbiota transplant has proved to be an extremely effective method for patients with recurrent infections with *Clostridium difficile*. We present the case of a 65-year-old female patient with multiple *Clostridium difficile* infection (CDI) relapses on the rectal remnant, post-colectomy for a CDI-related toxic megacolon. The patient also evidenced associated symptomatic *Clostridium difficile* vaginal infection. She was successfully treated with serial fecal “minitransplants” (self-administered at home) and metronidazole ovules.

Key words: *Clostridium difficile* infection – fecal microbiota transplant – rectal remnant – post-colectomy.

Abbreviations: GI: gastrointestinal; MRI: magnetic resonance imaging; CDI: *Clostridium difficile* infection; FMT: fecal microbiota transplant.

INTRODUCTION

The changes in the epidemiology of *Clostridium difficile* infection (CDI) during recent years, with increases in incidence and severity of the disease have made CDI a global public health challenge [1]. The rate of relapses after an initial treatment with metronidazole +/- vancomycin for a first CDI episode is between 15 and 30% [2]. The relapses are treated with other antibiotics (metronidazole, oral vancomycin, fidaxomicin), or with decreasing doses of vancomycin. After a first episode of relapse, up to 40% of the patients present a second relapse episode and have up to 65% chances for a third relapse [2]. The fecal microbiota transplant (FMT), often called ‘fecal transplant’ has emerged in the past years as an extremely effective method of treatment, with a rate of curability of over 90% for patients with multiple relapses [3].

We present the case of a 65-year-old female patient with multiple CDI relapses on the rectal remnant, preserved after a colectomy for a CDI-related toxic megacolon. The patient also had an associated symptomatic *Clostridium difficile* vaginal infection. She was successfully treated with serial fecal “minitransplants” (self-administered at home) and metronidazole ovules.

CASE PRESENTATION

A 65-year-old female admitted to the cardiology department for pulmonary valve endocarditis was treated intravenously with ceftazidime and vancomycin. She started to present 4-5 watery stools daily and fever spikes. Her past medical history was significant for hysterectomy with bilateral adnexectomy for uterine fibroma 20 years ago, breast cancer 4 years ago (treated by surgery, adjuvant chemotherapy and on-going hormonal therapy with anastrozole) and type 2 diabetes mellitus, requiring insulin over the last 5 years. The high clinical suspicion of CDI was confirmed by the positivity of A and B toxins in the stool diagnosed by an enzyme immunoassay test. Under orally administered metronidazole and vancomycin, the patient’s clinical and biological status deteriorated. A lower distal fecal microbiota transplant was performed, with her husband as the donor. The patient’s evolution did not improve and an abdominal x-ray revealed the aspect of toxic megacolon. A decision was made for surgical intervention. Ileostomy and colectomy with preservation of the rectum were performed, followed by a favorable evolution. A longer rectal remnant was preserved because the intra-operative situation permitted

Address for correspondence:

Daniel Popa
Polissano Clinic
24 Constitutie Str,
Sibiu, Romania
popadaniel1980@yahoo.com

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and with the prospect of a subsequent restoration of bowel continuity, which was postponed by the patient.

Twelve months after the surgical intervention, the patient started to present 2-3 emissions of rectal secretions daily. A proctoscopy was performed, that revealed partial disappearance of the vascular pattern, edema, mucosal erythema, small erosions, whitish secretions that could be easily removed by washing, not causing ulcerations (Fig. 1).



Fig. 1. Pre-fecal transplant rectum: partial disappearance of the vascular pattern, edema, erythema, small erosions, whitish secretions.

The A and B *Clostridium difficile* toxins from the secretions eliminated from the anus were found positive, but those from the stools collected through the ileostoma were negative. Initially vancomycin 4 x 250 mg/day was administered in rectal instillations for 10 days, and the patient became asymptomatic. After two weeks, the emission of rectal secretions relapsed and therapy with vancomycin 4 x 250 mg/day was resumed for 10 days followed by a fecal transplant at 36 hours after the completion of antibiotic treatment. The patient's daughter was this time the donor; an endoscopic instillation of approximately 100 ml of fresh stools was made, partially discharged during the procedure.

The patient remained asymptomatic for a month and then presented rectal secretions associated with a small amount of vaginal secretions. Testing for A and B *Clostridium difficile* toxins from both the rectal and vaginal secretion harvested on a swab by the gynecologist was positive. In order to explore a possible recto-vaginal fistula, 20 ml of saline + methylene blue were instilled rectally, which did not externalize at the vaginal level. Nevertheless, a pelvic MRI scan was also performed which showed no signs of fistula. A decision was made to initiate a therapy with metronidazole ovules for 7 days and to restart vancomycin therapy 4 x 250 mg in rectal instillations for 10 days.

As the patient used to work in the healthcare system, she was trained to perform serial fecal "ministransplants" (enemas) at home with the daughter as donor. At least 50 g of freshly harvested stools were mixed in a tight container with 250 ml of

saline. The content was vigorously shaken for several minutes and then passed through several layers of gauze into another container; 20 ml of suspension were instilled during the first transplant, performed at 36 hours after the completion of the antibiotic treatment, using a rectal tube. The patient was advised to lie down on the bed after instillation and to rest like this as much as possible. All the instruments used were of single use. In total, four fecal "minitransplants" were performed, at 2 days intervals. At transplants 2-4, observing that the patient could retain the suspension for 4 hours, we increased the instilled volume at 30 ml/session, with a minimum of 2 hours retention.

The patient did not complain of any side effects, she did not have further emissions of vaginal or rectal secretions and she has remained asymptomatic for 6 months since the last transplant. Endoscopic examination at 3 months post-transplant revealed minimum edema, vascular pattern present, no erosions or ulcerations (Fig. 2).

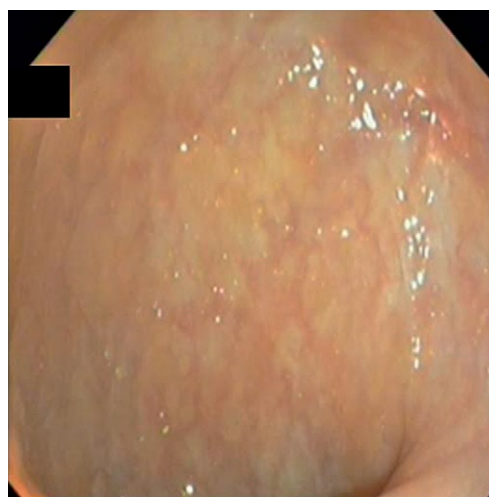


Fig. 2. Post-fecal transplant rectum (3 months): vascular pattern present, minimum erythema, no erosions or ulcerations.

DISCUSSION

The first documentary evidence regarding the use of a human fecal suspension for the treatment of severe forms of diarrhea dates back to the 4th century in China [4]. Although the FMT was used empirically to treat various forms of diarrhea during centuries, it has gained ground in the past few years as a treatment with a curability rate of over 90% for patients with multiple relapses [3] or in severe cases of CDI [5].

There is no consensus on the administration methodology, as there are several methods of instillation for the fecal suspension: proximal lower gastrointestinal (GI) FMT (colonoscopic method), distal lower GI FMT (via enema/rectal tube) and upper GI FMT (nasogastric tubes, duodenal tubes, via endoscope). Also, there is no consensus on the screening of donors, pre-transplant preparation, post-transplant protocol, on the quantity of stools transformed into a suspension in order to be administered, but the therapeutic results have led to the increased widespread use of this technique for the treatment of patients with multiple relapses of CDI [6].

Distal lower GI tract FMT requires smaller volumes of fecal suspension administered through enemas, retention enemas or rectal tubes, whether in one session or in consecutive sessions; distal lower GI FMT may also be used in combination with another administration route, the proximal lower GI FMT [7]. The advantages of this method are: lower costs, less invasiveness, not requiring special endoscopic skills as it may be administered in out-patient units, self-administered by patients at home or by family members thus allowing a greater access of patients to FMT. Silverman et al. reported seven cases of CDI successfully treated through self-administration or by family member administration of the fecal suspension at home, by enemas [8].

Post-colectomy CDI manifests variably from asymptomatic forms to severe forms of infection; *Clostridium difficile* enteritis is a rare disease, while *Clostridium difficile* pouchitis has been reported in 10% of symptomatic cases at a referral center for pouch dysfunction [9].

The case of our patient stands out due to the symptomatic double localization of the CDI, respectively rectal and vaginal. O'Ferrall et al. reported a vaginal carriage rate of 11% in consecutive female patients attending a sexually transmitted diseases clinic and 18% in the case of pregnant women [10].

To the best of our knowledge, this is the first case reported of FMT successfully performed on a rectal remnant for multiple CDIs. After the failure of a fecal transplant using 100 ml suspension during one endoscopic session, it was decided to perform successive, self-administered "minitransplants" at home, at an interval of 2 days (considering the donor transit time), 4 sessions in total, with an increase of the instilled volume up to 30 ml due to the good tolerance of the patient. The serial administration method, in consecutive days or at short intervals (depending on the donor's rhythm of stools emission) proved to be efficient, considering that the instilled suspension volume was adapted to the largest volume tolerated by the patient for as long a period as possible.

CONCLUSION

Home self-administration of fecal "minitransplants" for recurrent *Clostridium difficile* infection on a rectal remnant should be considered an efficient therapeutic method.

Conflicts of interest: None to declare.

Authors' contribution: D.P. and L.C. wrote the manuscript. D.P., L.C., M.L. and O.P. diagnosed and treated the patient. E.U. established the gynecologic diagnosis. M.M. and O.P. reviewed the manuscript for its intellectual content. All authors read and approved the final version of the manuscript.

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