

Fecal Transplant Eliminates Persistent MDR Infection

Daniel M. Keller, PhD | October 20, 2014

PHILADELPHIA — Fecal microbiota transplantation successfully decolonized the gut of a young girl who persistently harbored multidrug-resistant *Klebsiella pneumoniae* bacteria, according to a case report.

The treatment is increasingly being used to manage recurrent or refractory *Clostridium difficile* infections, but this is the first instance of its use to decolonize carbapenem-resistant enterobacteriaceae and return normal flora to the gut, the researchers report.

The case of a 13-year-old girl with a history of recurrent otitis media and otomastoiditis whose operative cultures grew *Pseudomonas aeruginosa* was described here at IDWeek 2014 by Abigail Freedman, MD, attending physician at Alfred I. duPont Hospital for Children in Wilmington, Delaware.

The patient was treated with broad-spectrum antibiotics, but continued to have pain and positive superficial cultures. She was readmitted to the hospital a month later with a persistent fever and was diagnosed with hemophagocytic lymphohistiocytosis. She improved after treatment with high-dose corticosteroids and etoposide, and was discharged.

Two months later, after the onset of a new fever, her blood cultures revealed highly multidrug-resistant carbapenemase-producing *Klebsiella pneumoniae*. Antibiotics failed to clear the organism from her blood, and she developed septic arthritis in one shoulder and both hips.

With just about no antibiotic choices left, Dr Freedman turned in desperation to the Internet for help and, she said, "a wondrous group of consultants came forth to help." Suggestions of an extended infusion of doripenem, colistin, rifampin, and plazomicin (an aminoglycoside in phase 3 trials) controlled the bloodstream infection. The patient's joints were washed out with polymyxin.

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But the possibility of persistent colonization with carbapenemase-producing *Klebsiella pneumoniae* and the re-emergence of active infection when antibiotics were stopped loomed because of the patient's underlying hemophagocytic lymphohistiocytosis and immunosuppression from heavy steroid therapy.

Although she remained asymptomatic for several months, carbapenemase-producing *Klebsiella pneumoniae* was found in her stool, and 7 months after stopping antibiotics, she developed severe osteomyelitis of the femur with the same organism. At that point, she underwent fecal transplantation.

A younger, healthy, fully immunized, antibiotic-free half-brother became the donor after his stool tested negative for bacteria and viruses of concern and for ova and parasites. Donor stool (25 to 30 g) was homogenized in 60 mL normal saline in a Hamilton Beach Personal Blender. The homogenate was then filtered twice through commercially available unbleached coffee filters.

"The procedure itself took less than 10 minutes — after hours of preparation — and was very simple and benign," Dr Freedman reported. Using a nasoduodenal tube, 25 mL of filtrate was administered, and the patient remained in a semi-upright position for an hour after the procedure. She reported only mild transient nausea and experienced no complications.

"Two weeks after the transplant, carbapenem-resistant enterobacteriaceae *Klebsiella* was not detectable in a stool sample, and remained undetectable in 4 stools over the next 8 months," Dr Freedman explained. "There was no further clinical evidence of bacterial infection."

The patient is now 18 years old and her hemophagocytic lymphohistiocytosis is in remission. Unfortunately, she will need bilateral hip replacements because of aseptic necrosis, and she still has some psychological adjustment problems because of her long ordeal, Dr Freedman told to *Medscape Medical News*.

It is not clear whether the donor has to be a family member, or whether a defined mixture of bacteria would work as well as stool, Dr Freedman added.

She advised that for patients with extremely abnormal fecal flora related to the antibiotic-induced selection of highly resistant bacteria, clinicians should consider fecal transplantation to repopulate the colon and achieve a more normal fecal microbiome.

How the benefits of transplantation accrue is not exactly known. "We know it works, but we really don't understand how it works," said Mary Hayden, MD, professor of medicine at the Rush University Medical Center in Chicago, who was IDWeek program committee chair and was not involved in the study.

It might be a combination of good bacteria outcompeting bad bacteria, plus some host-microbiome interaction, she speculated during a news briefing.

A Simpler, Less Icky Method of Transplant

A poster reporting on the use of orally administered capsules of cryopreserved, concentrated, fecally derived bacteria to treat recurrent *C difficile* infection resistant to more conventional treatment was presented by Nimit Saraiya, MD, an infectious disease fellow at the Hofstra North Shore-LIJ Health System in Manhasset, New York.

Donors were in good health, were screened for infectious diseases, and had not received any antibiotics in the previous 6 months. The processed donor material was triple-encapsulated to allow intact organisms to reach beyond the stomach.

In an outpatient setting, 13 women and 6 men swallowed approximately 10 capsules. The clinical end point was the resolution of *C difficile* infection without relapse for 90 days. The patients were treated with oral vancomycin until the day before transplantation, and received omeprazole the night before and the morning of the transplantation.

After the ingestion of one regimen, the *C difficile* infection resolved in 13 patients (68%). After a second ingestion, four more patients responded. Further ingestions were not effective for the remaining two patients.

There were five instances of transient epigastric discomfort but, in general, patients tolerated the treatment well.

"We found that people did just as well as previous studies have shown with the more invasive ways of transplanting, which is either endoscopy or colonoscopy," Dr Saraiya told *Medscape Medical News*. "Within about 3 days, we saw that patients achieved symptomatic improvement in terms of the diarrhea."

The researchers conclude that the oral capsule "offers an aesthetic, noninvasive, effective, and cost-efficient option for the treatment of recurrent and persistent *C difficile* infection."

Fecal transplantation is certainly not standardized at this point. "People are just kind of doing this on their own," said Erik Dubberke, MD, associate professor of medicine at Washington University in St. Louis, who was not involved in the studies.

Although there are recommendations, practitioners have their own methods for donor screening, specimen processing, and administration. It is left up to each institution whether the procedure is considered standard of care for persistent *C difficile* infection, and whether Institutional Review Board approval is required, Dr Dubberke explained.

He said he agrees that the mechanism of action is not clear. "Direct suppression somehow, stimulation of the immune system, competition for nutrients or binding sites, and metabolic processes that give the good bacteria an advantage and the bad bacteria a disadvantage" are all possibilities, he noted.

Dr Freedman, Dr Hayden, and Dr Saraiya have disclosed no relevant financial relationships. Dr Dubberke reports being a consultant for and enrolling patients in trials conducted by Rebiotix.

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