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MAJOR ARTICLE

Fecal Microbiota Transplantation in Patients With Blood Disorders Inhibits Gut Colonization With Antibiotic-Resistant Bacteria: Results of a Prospective, Single-Center Study

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Background. Patients with blood disorders colonized with antibiotic-resistant bacteria (ARB) are prone to systemic infections that are difficult to treat. Reintroduction of commensal bacteria in a murine model of enterococcal colonization of the gut can lead to eradication of enterococci. We hypothesized that fecal microbiota transplantation (FMT) could be used to eradicate ARB in humans.

Methods. Participants colonized with ARB were treated with intraduodenal FMT according to a prospective protocol (NCT02461199). The primary endpoint was complete ARB decolonization at 1 month after FMT. Secondary endpoints included safety assessment and partial ARB decolonization. Microbiome sequencing was performed to investigate the influence of microbial composition of the transplanted material on the outcome of FMT.

Results. Twenty-five FMTs were performed in 20 participants (including 40% who had neutropenia) who were colonized by a median of 2 (range, 1–4) strains of ARB. The primary endpoint was reached in 15/25 (60%) of the FMTs and more frequently in cases in which there was no periprocedural use of antibiotics (79% vs 36%, $P < .05$). Among participants, 15/20 (75%) experienced complete ARB decolonization. There were no severe adverse events, and partial ARB decolonization was observed in 20/25 (80%) of the FMTs. The microbiota composition analysis revealed higher abundance of *Barnesiella* spp., *Bacteroides*, and *Butyricimonas* and greater bacterial richness in the fecal material, resulting in eradication of *Klebsiella pneumoniae* compared with nonresponders.

Conclusions. FMT in patients with blood disorders is safe and promotes eradication of ARB from the gastrointestinal tract.

Clinical Trials Registration. NCT02461199.

Keywords. fecal microbiota transplantation; antibiotic-resistant bacteria; gut colonization; hematology; infection.

In recent years, the World Health Organization and the scientific community have expressed alarm at the increasing rates of antimicrobial resistance. This increase has been caused by the extensive use of broad-spectrum antibiotics, and antimicrobial resistance is now considered to be one of the most critical threats to human health [1, 2].

Recent studies have revealed that the commensal microbiota in the human gut act as a large reservoir of antibiotic-resistance genes [3, 4]. The natural, healthy microbiome prevents the colonization of gastrointestinal (GI) niches by pathogens, which is known as colonization resistance. However, this crucial defense mechanism can be impaired by treatment with antibiotics and chemotherapy [5], and people may consequently become carriers of pathogenic bacteria, including strains that are resistant to treatment.

Colonized patients pose an epidemiological threat to other hospitalized individuals and to members of their households [6, 7] but are also in danger of developing systemic infections with gut-colonizing microorganisms [8, 9]. This is especially the case for patients with blood disorders due to suppression of their innate and/or acquired immunity. It has been reported that 70% of cases of bacteremia in individuals with hemato-oncological diseases are derived from the gut [9]. Systemic infections with antibiotic-resistant bacteria (ARB; eg, carbapenem-resistant *Acinetobacter baumannii* and carbapenem-resistant *Pseudomonas aeruginosa*) in patients who have undergone allogeneic hematopoietic cell transplantation (alloHCT) are associated with a mortality rate of 36%–95% [10–12].

Fecal microbiota transplantations (FMTs) are increasingly being carried out in clinical practice to restore the physiological composition of the gut microflora. FMT has become a standard

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treatment for relapsing *Clostridium difficile* infection and it is associated with a cure rate of >90% [13]. Furthermore, it is increasingly being used as a novel treatment for diseases that are linked with pathological imbalances of the microbiome, including inflammatory bowel diseases, obesity, and metabolic and rheumatoid diseases [14]. Recently it was shown that FMT in a murine model of vancomycin-resistant enterococci (VRE) gut colonization can lead to eradication of VRE [6]. It is likely that restoration of gut biodiversity and introduction of specific strains of commensal bacteria can displace pathogenic strains, leading to decolonization.

We hypothesized that FMT can eradicate ARB in the human gut in a manner that is similar to how FMT works in *C. difficile* infection and in a murine model of VRE colonization of the gut. After an initial successful attempt [15], we carried out a prospective study to assess use of the procedure in individuals with blood disorders.

METHODS

Study Design

In this single-center, prospective study, we collected data on 25 FMTs performed in participants whose GI tracts were colonized with ARB. The FMTs were performed between February 2015 and July 2016 at the Department of Hematology, Oncology, and Internal Diseases of the Medical University of Warsaw, Poland.

The primary endpoint of the study was complete ARB decolonization at 1 month after FMT. Secondary endpoints included safety assessments and partial ARB decolonization. Gut decolonization was defined as a negative result for a minimum of 2 consecutive rectal swab cultures. However, in cases that involved carbapenemase-producing *Enterobacteriaceae* (CPE), a negative result of a quantitative real-time polymerase chain reaction (qPCR) test for an antibiotic-resistance gene encoding carbapenemase was also required. Complete ARB decolonization was defined as decolonization of all strains of ARB, while partial ARB decolonization was defined as decolonization of at least 1 strain of ARB.

Treatment Protocol

Details of the treatment protocol are provided in the Supplementary Materials. FMT was offered to consecutive adult patients whose GI tracts were colonized with ARB and who did not meet exclusion criteria. The participants consented to FMT and allowed the resultant data to be analyzed and published. The Medical University of Warsaw Ethics Committee approved the research protocol (KB/180/2014).

The transplanted fecal material was obtained from healthy unrelated donors who underwent thorough clinical examinations and antimicrobial testing [13]. Each FMT product was derived from 100 g feces. The day before FMT, bowel lavage was carried out using macrogols. Each participant fasted for at least 12 hours before transplantation, and a proton pump inhibitor was administered in the evening before FMT and twice daily on the day of transplantation to neutralize gastric acid.

Each FMT was carried out intraduodenally via a nasoduodenal tube. The first 3 participants underwent FMT on a single day, while the remaining participants underwent FMT on 2 consecutive days. Routine on-ward monitoring was performed for the subsequent 2 days. FMT efficacy was assessed by culturing rectal swabs obtained 1 week, 1 month, and 6 months after FMT. In cases that involved colonization with CPE, fecal samples were also tested using qPCR for the presence of an antibiotic-resistance gene encoding carbapenemase. Additional fecal samples were collected and frozen in liquid nitrogen for subsequent microbiome sequencing.

Next-Generation Sequencing

From 7 patients colonized with *K. pneumoniae*, New Delhi metallo-β-lactamase-1 (NDM1+) fecal samples were subjected to microbiota composition sequencing. DNA was extracted and the V3–V4 region of the 16S rRNA gene was sequenced using an Illumina MiSeq Desktop Sequencer. Based on the available literature data, several genera were selected and subjected to detailed analysis as likely to be involved in the decolonization of ARB (*Barnesiella*; *Bacteroides*; *Butyricimonas*; *Clostridium IV*, *XIVa*, and *XIVb*; and *Lactobacillus*; see Supplementary Materials).

Statistical Analyses

The 64-bit versions of USEARCH [16] and mothur [17] were used in combination with several in-house programs for bioinformatical analysis of the microbiome sequence data (see the Supplementary Materials). Statistical analysis of the clinical data was conducted using STATISTICA 10 for Windows and R Statistics. Abundance of taxa between groups was evaluated with *t* tests on square-root transformed data; assumptions of variance homogeneity were tested with an *F* test (Welch *t* test [Welch unequal variances *t* test] was used when this assumption was not met).

RESULTS

Patients Characteristics

Overall, 20 patients with blood disorders were enrolled in the study and underwent 25 FMTs. Although most individuals underwent only 1 FMT, 3 underwent 2 and 1 underwent 3. A summary of the participants' clinical characteristics is provided in (Table 1); detailed case-by-case characteristics are provided in (Supplementary Table 2s). The gut-colonizing ARB included *K. pneumoniae* NDM1+ (n = 14), carbapenem-resistant *K. pneumoniae* (n = 3), *K. pneumoniae* extended-spectrum β-lactamase positive (ESBL+; n = 2), *Escherichia coli* ESBL+ (n = 11), *Pseudomonas aeruginosa* metallo-β-lactamase (MBL; n = 2), carbapenem-resistant *P. aeruginosa* (n = 2), carbapenem-resistant *Enterobacter cloacae* (n = 2), VRE (n = 2), and other strains of ARB (n = 3; Table 3). Thirteen participants (52%) were colonized

Table 1. Baseline Demographic Characteristics of the Study Sample

Characteristic	No.	Median (Range)	% of FMTs
Participants	20		
FMTs	25		
Participants who underwent 2/3 FMTs	3/1		
Male sex	14		56
Age at FMT (y)			
Median		51	
Range		22–77	
ANC at FMT ($\times 10^9$/L)			
Median		2.1	
Range		0.5–16.5	
FMTs for participants with neutropenia (ANC 0.5–1.8 $\times$ 10^9/L)	10		40
Diagnosis			
Acute myeloblastic leukemia	5		20
Acute graft-versus-host disease	4		16
Chronic graft-versus-host disease	2		8
Multiple myeloma	3		12
Diffuse large B-cell lymphoma	2		8
Myelodysplastic syndrome	1		4
Lung cancer	1		4
Thrombotic thrombocytopenic purpura	1		4
Kidney transplant recipient	1		4
Strains of colonizing ARB (median, range)			
Median		2	
Range		1–4	
FMTs for participants with at least 2 strains of colonizing ARB	13		52
Colonization assessment at 1 week after FMT	25		100
Colonization assessment at 1 month after FMT	24		96
Colonization assessment at 6 months after FMT	14		56
Follow-up period (days; mean, range)			
Median		187	
Range		9–482	

Abbreviations: ANC, absolute neutrophil count; ARB, antibiotic-resistant bacteria; FMT, fecal microbiota transplantation.

with at least 2 strains of ARB (range, 1–4). The median neutrophil count immediately prior to FMT was 2.1 $\times$ 10^9/L (range, 0.5–16.5 $\times$ 10^9/L), and 40% of participants had neutropenia (<1.8 $\times$ 10^9 neutrophils/L), but not severe neutropenia (<0.5 $\times$ 10^9/L).

Outcomes

The microbiological follow-up data were available for all FMTs at the 1-week time point and for 24/25 of the FMTs at the 1-month time point (1 participant died from primary disease within the first month post-FMT). Additionally, for 14 FMTs, there were follow-up data for the 6-month time point. qPCR testing for an antibiotic-resistance gene was performed for 17 participants at 1 month and for 9 participants at 6 months.

Complete ARB decolonization was achieved in 15/25 (60%) of the FMTs at 1 month and in 13/14 (93%) of the FMTs at 6 months (Table 2). Complete ARB decolonization was achieved in 15/20 (75%) of the participants (taking into account the participants who underwent repeated FMTs). Partial ARB decolonization was achieved in 20/25 (80%) cases at 1 month and in 13/14 (93%) cases at 6 months. Notably, among the patients who received 1-day FMTs (n = 3), no cases of complete ARB decolonization occurred, and only 1 participant achieved partial ARB decolonization at 1 month.

For 17 patients, qPCR was used to investigate whether ARB with a gene encoding carbapenemase were eradicated. Results were negative in 9/17 (53%) individuals at 1 month and in 8/9 (89%) participants at 6 months. The results for each case of ARB colonization were analyzed separately (Table 3).

The most abundant pathogen was *K. pneumoniae*, and it was found to be eradicated in 10/19 (53%) FMTs at 1 month, which included 6/10 (60%) cases involving *K. pneumoniae* NDM1+. There was higher efficacy associated with eradication of *E. coli* ESBL+ (n = 11) and *E. coli* oxacillinase-48 (OXA-48+; n = 1); the rate of eradication of these strains was 100% at 1 month.

Clinicians were permitted to administer antibiotics based on clinical need. We analyzed patients who had antibiotics introduced in the first 7 days after FMT (11/25 [44%] cases). Complete ARB decolonization was achieved in a significantly higher proportion of FMTs that did not involve antibiotics (11/14, 79%) compared with those that did involve antibiotics (4/11; 36%, $P = .039$). The rates of partial ARB decolonization were also higher: 13/14 (93%) of the FMTs that did not involve antibiotics vs 7/11 (64%) of those that did involve antibiotics, but the difference was not significant.

Safety Assessment

The mean follow-up period was 187 days (range, 9–482 days). FMT was found to be safe; the adverse events were either mild and transient or exacerbations of conditions that were already present before the FMTs (Table 4). During the follow-up period, 1 previously decolonized patient experienced sepsis as a result of a persisting skin infection caused by *P. aeruginosa* MBL+. Another participant with severe chronic graft-versus-host disease died within the first month post-FMT as a result of septic shock caused by *E. coli* OXA-48+, which had previously been eliminated from the GI tract. In 2 participants, recolonization with the same strain of ARB was observed at about 1 and 6 months after decolonization, respectively. In 1 patient, *K. pneumoniae* MBL+ was decolonized, but a new species (*Pseudomonas rhodesiae*) that exhibited the same resistance mechanism colonized the gut. More information about each FMT is provided in the Supplementary Materials.

Microbiome Analyses

Of the 7 patients colonized with *K. pneumoniae* NDM1+ whose microbiota compositions were analyzed, 4 became decolonized,

Table 2. Impact of Fecal Microbiota Transplantation on Complete and Partial Antibiotic-Resistant Bacteria (ARB) Decolonization, With or Without Antibiotics During the First Week After Transplantation

	All FMTs n = 25		With Antibiotics, n = 11		Without Antibiotics, n = 14		
Endpoint	No.	%	No.	%	No.	%	*P* Value
Effect on all strains of ARB per FMT (complete ARB decolonization)							
At 1 month	15/25	60	4/11	36	11/14	79	.039
At 6 months	13/14	93	4/5	80	9/9	100	.037
Effect on at least 1 strain of ARB per FMT (partial ARB decolonization)							
At 1 month	20/25	80	7/11	64	13/14	93	NS
At 6 months	13/14	93	4/5	80	9/9	100	–

Abbreviations: ARB, antibiotic-resistant bacteria; FMT, fecal microbiota transplantation.

Table 3. Decolonization of Particular Strains of Antibiotic-Resistant Bacteria in All Participants and Those Without Antibiotics Use During the First Week After Fecal Microbiota Transplantation

	Negative Rectal Swab at 1 Week				Decolonization at 1 Month			
	All		Without Antibiotics		All		Without Antibiotics	
Pathogen	No.	%	No.	%	No.	%	No.	%
Klebsiella pneumoniae								
New Delhi metallo-β-lactamase 1	8/14	57	6/6	100	6/10	60[a]	5/6	83[a]
Other, carbapenem-resistant	2/3	67	2/2	100	3/3	100	2/2	100
ESBL+	1/2	50	0/1	0	1/2	50	1/1	100
Escherichia coli								
ESBL+	11/11	100	3/3	100	11/11	100	3/3	100
OXA-48 – extended-spectrum oxacillinase-48	1/1	100	1/1	100	1/1	100	1/1	100
Pseudomonas aeruginosa								
MBL+	2/2	100	2/2	100	2/2	100	2/2	100[a]
Other, carbapenem resistant	1/2	50	1/2	50	2/2	100	2/2	100
Carbapenem-resistant *Enterobacter cloacae*	1/2	50	1/2	50	2/2	100	2/2	100
Vancomycin-resistant enterococci	2/2	100	1/1	100	2/2	100	1/1	100
Acinetobacter ursingii MBL+	1/1	100	1/1	100	1/1	100[a]	1/1	100[a]
Stenotrophomonas maltophilia	1/1	100	1/1	100	1/1	100	1/1	100

Abbreviations: ESBL, extended-spectrum β-lactamase; MBL, metallo-β-lactamase.

[a]Decolonization confirmed by quantitative real-time polymerase chain reaction.

while the remaining 3 were nonresponders. The fecal material transplanted into the responders had a higher abundance of *Barnesiella* spp. (1.3% vs 0.2%, *P* = .009), *Bacteroides* (12% vs 0.7%, *P* = .008), and *Butyricimonas* (0.1% vs 0%, *P* = .016; Figure 1A-C) and a higher number of operational taxonomic units (OTUs; 176 vs 122, *P* = .003; Figure 1D) compared with the material used from nonresponders. There was no significant difference in the diversity of the microbiome in the fecal material transplanted into the responders and nonresponders (Shannon index: 3.5 vs 3.1, *P* = .06; Figure 1E). There were no significant differences between the responders and nonresponders in the abundance of *Barnesiella* spp., *Bacteroides*, *Butyricimonas*, the number of OTUs, or the Shannon index of fecal samples taken from the participants before and after FMT (see Supplementary Materials).

Table 4. Adverse Events After Fecal Microbiota Transplantation

Event	No.	%	Comment
Vomiting	1	4	Immediately after infusion
Diarrhea within 3 days after FMT	25	100	Grade 1, transient
Abdominal pain	2	8	Grade 3, present already before FMT
Ileus	2	8	Grade 2, present already before FMT

Safety assessment of the adverse events involved grading them [18].

Abbreviation: FMT, fecal microbiota transplantation.

DISCUSSION

Recently we showed that individuals who underwent alloHCT and who were colonized with ARB had a higher mortality rate

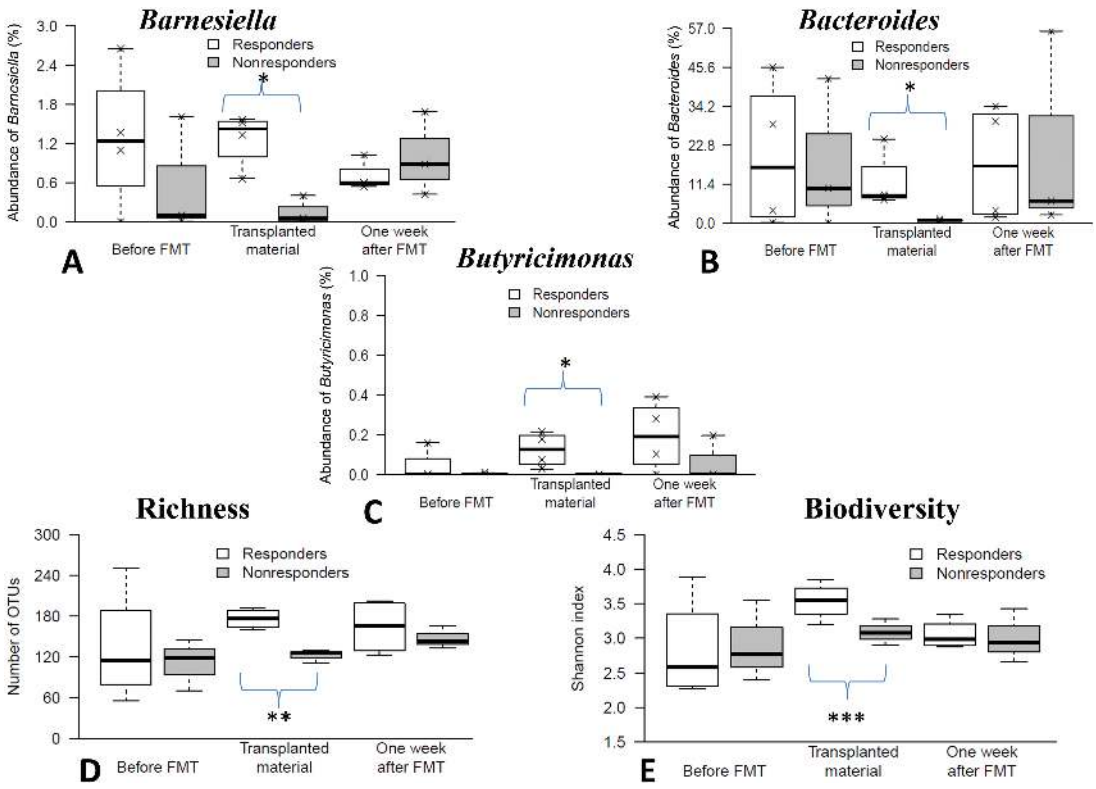

Figure 1. Analysis of next-generation sequencing data from samples obtained from the transplanted fecal material donated to patients who were colonized with *Klebsiella pneumoniae* NDM1+. The white bars represent participants who were decolonized after fecal microbiota transplantation (n = 4), and the gray bars represent participants who were not decolonized (n = 3). *A,* Proportion of *Barnesiella* spp. in the samples. **P* = .009. *B,* Proportion of *Bacteroides* in the samples. **P* = .008. *C,* Proportion of *Butyricimonas* in the samples. **P* = .016. *D,* Richness of the microbiome, as assessed using the number of operational taxonomic units. ***P* = .003. *E,* Diversity of the microbiome, as assessed using the Shannon index. ****P* = .06. The box excludes the upper and lower 25% (quartiles) of data; the lines go to maximum and minimum excluding outliers. Outliers are defined as more/less than 3/2 of the upper/lower quartile. The line is the median. All data points are marked with "x" in the box plots. Abbreviation: FMT, fecal microbiota transplantation.

from infection (42% vs 11%, $P < .05$), higher nonrelapse mortality (37% vs 9% at 1 year after alloHCT, $P = .001$), and lower overall survival rate (53% vs 81%, $P < .001$) compared with not colonized individuals [12]. There have been recent reports of the negative effect of decreases in the heterogeneity of the gut microbiome on survival related to increased transplant-related mortality [19], and these observations may have a causal relationship. It is also clear that gut colonization in patients with hematological diseases is associated with an increased rate of life-threatening systemic infections [9–12]. We postulated that restoration of the physiological composition of gut flora using FMT may benefit individuals with blood disorders and clear the gut from ARB.

The literature suggests that spontaneous decolonization is a long process. Most data come from analyses of patients treated in long-term care facilities and intensive care units. In a study by O'Fallon et al, the median duration of colonization with multidrug-resistant gram-negative bacilli was 144 days [20]. The spontaneous clearance of all resistant strains occurred in only 9% of participants. In addition, Haverkate et al found that the median time to spontaneous decolonization of ARB in intensive care unit patients was 4.8 months [21], and patients hospitalized in long-term acute-care hospitals needed a median of 205 days (and 270 days between readmissions) to get rid of colonizing ARB strains [22]. Looking at analyses performed in populations that are more comparable to the population in our study, the median duration of colonization with VRE in pediatric oncology patients was 112 days [23] and 306 days in immunosuppressed liver or kidney transplant recipients colonized with VRE [24]. In a population that included patients with blood disorders, Zimmerman et al reported that a longer time (mean 387 days) was required to obtain negative rectal swab cultures from individuals who were originally colonized with CPE [25]. These findings were confirmed by Oren et al who revealed that only 7% of patients on a hematology ward became decolonized from CPE after a median of 140 days [26].

Also there have been attempts to decolonize patients using targeted antibiotics. For this reason, patients were treated with oral rifaximin, polymyxin B, colistin, or aminoglycoside. Rieg et al showed that treatment led to the eradication of ESBL+ *Enterobacteriaceae* in 42% of individuals. However, 54% of them were recolonized within 3 months [27]. A double-blind, placebo-controlled study showed that oral colistin

plus neomycin significantly lowered the rectal carriage of ESBL+ *Enterobacteriaceae* from the first day of treatment. However, this effect disappeared 1 week after treatment was completed [28]. In contrast, more encouraging results were found in a study that assessed the efficacy of oral gentamicin plus polymyxin B for the eradication of carbapenem-resistant *K. pneumoniae* [29]. One week after treatment ended, 16% of rectal swab cultures in the placebo arm and 61% in the treatment arm were negative ($P < .01$), and a difference was maintained at 5 weeks after treatment was completed. Although the use of oral antibiotics to decontaminate the GI tract may lead to decolonization, there is a strong rationale for not using this treatment in clinical practice. Namely, it has been documented that use of this antibiotic to decontaminate the GI tract leads to the emergence of colistin resistance [30].

In our study, we assessed the potential for using FMT to tackle colonization of the gut by ARB in patients with blood disorders. The participants were colonized with heterogeneous strains of ARB; 19 with *K. pneumoniae*, including 14 with the highly antibiotic-resistant strain NDM1+, and 11 with *E. coli* ESBL+. The participants had impaired immunity, and the majority had neutropenia (but not severe neutropenia of $<0.5 \times 10^9$/L). Traditionally, the introduction of fecal isolates into the GI tracts of immunocompromised individuals has been considered dangerous. However, there is strong evidence that the systemic infections experienced by this patient group are caused not by commensal gut microflora but by pathogenic bacteria acquired from other patients due to the loss of colonization resistance [31]. There is increasing acceptance that the traditional low microbial diet (the "neutropenic diet") may not be appropriate for these individuals [32] and that treatment with probiotics may be beneficial [33].

We carried out FMT with a high degree of caution. Each fecal microbiota suspension was administered via a nasoduodenal tube (which was localized using X rays) to avoid aspiration of the suspension. The initial 3 participants underwent a 1-day FMT and, as no unwanted effects were observed, the remainder of the participants underwent a 2-day FMT. The participants were strictly monitored while they stayed in hospital and were also followed up after discharge. There were no systemic infections shortly after FMT. Moreover, FMT appeared to be highly efficient at eradicating ARB from the GI tract. Complete ARB decolonization was observed at 1 month in 60% of the FMTs, which is higher than the rates of spontaneous and oral antibiotic–induced decolonization, as discussed above. The rate of partial ARB decolonization was even higher, at 80%. The reported results are in line with recent observations by Millan et al who reported that FMT used to treat recurrent *C. difficile* infection reduces the load of antibiotic-resistant genes in the gut of patients heavily pretreated with antibiotics [34].

Another positive aspect of the FMTs was the durability of the response, that is, recolonization with the same ARB occurred in only 3/15 (20%) patients (see Supplementary Materials). It should be noted that the efficacy of FMT at eradicating *E. coli* ESBL+ from the GI tract was 100%. In patients colonized with highly resistant *K. pneumoniae* NDM1+, complete ARB decolonization was achieved in 60% of cases and in 83% of patients not treated with antibiotics for the first week post-FMT, confirmed by qPCR.

One putative mechanism of action of FMT against ARB is restoration of heterogeneity in the gut microbiota, including the restoration of species that tend to occupy the physiological niches that had been taken over by the ARB, eventually leading to eradication of the latter. Our data show that administration of antibiotics within 1 week of FMT radically decreases the efficacy of the procedure. When antibiotics were not used, the rate of complete ARB decolonization reached 79% compared with 36% when antibiotics were administered. This is certainly in line with our theory, as antibiotics presumably act against the transplanted physiological microflora, thus diminishing their effect. Therefore, when possible, the use of antibiotics shortly after FMT should be reserved for life-threatening situations.

To explore the mechanisms behind the effects of FMT, we performed next-generation sequencing (NGS) of fecal samples taken from patients who were colonized with *K. pneumoniae* NDM1+ and from the fecal material that was transplanted into them. Regarding the transplanted fecal material, the number of OTUs was significantly higher in the fecal material that was donated to the responders compared with that from nonresponders. We found that *Bacteroides* and *Butyricimonas* (common anaerobes) were more abundant in fecal material given to responders than to nonresponders. Even more intriguing was the observation that the fecal material used in cases in which *K. pneumoniae* NDM1+ was eradicated had a higher abundance of *Barnesiella* spp. than the material used in cases in which *K. pneumoniae* was not eradicated.

Ubeda et al found that in a murine model, restoration of *Barnesiella* spp. following FMT was associated with elimination of VRE [6]. Recently, Caballero et al showed that VRE occupies niches in the GI tract that overlap spatially with those occupied by *K. pneumoniae* [7]. Our finding, although it relates to a small number of observations, suggests that a high abundance of *Barnesiella* spp., *Bacteroides*, and/or *Butyricimonas* and/or a large number of OTUs in the transplanted fecal material contribute to the eradication of *K. pneumoniae*. This suggests that the composition of the transplanted fecal material affects the outcomes of FMT.

Our study had several limitations. First, we were unable to control the use of antibiotics, which affected the efficacy of the procedure. In addition, the strains of ARB that colonized participants were heterogeneous. However, our cohort included a large number of participants who were colonized with the highly antibiotic-resistant *K. Pneumoniae* NDM1+, which poses one of the most severe epidemiological threats. We are also aware that this was a single-arm study, without an adequate control group, which makes the interpretation of results difficult. Therefore, it should be primarily treated as a feasibility study that evaluated the safety and

preliminary efficacy of the procedure, the results of which can be interpreted only based on literature data. Future approaches should focus on more advanced, placebo-controlled phase 2 and 3 clinical trials that include groups, allowing reliable statistical comparisons.

In conclusion, we clearly show that FMT is a safe procedure for patients with blood disorders. FMT promoted decolonization of most participants, although administration of antibiotics shortly after FMT decreased the success rate. We also show that eradication of *K. pneumoniae* may depend on the abundance of *Barnesiella* spp., *Bacteroides*, and/or *Butyricmonas* in the transplanted fecal material. FMT appears to constitute a valid tool for tackling colonization of the gut by ARB in patients with blood disorders.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. J. B., G. W. B., P. G., and W. W. J. designed the study. J. B. and K. R. collected the data, and J. B., G. W. B., and N.S. analyzed the data. All the authors vouch for the accuracy of the data and approve of the analysis. M. W., G. D., T. D., J. D. T., and P.G. devised the microbiological protocol. J. B. , G. W. B., and N. S. were the primary authors of the article, but all the other authors contributed to it.

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