Comparing Different Delivery Methods of Fecal Microbiota Transplantation

oral capsule, oesophagogastroduodenoscopy, colonoscopy, and gastric tube

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Background/Aims

The increasing prevalence of multidrug-resistant organism (MDRO) carriage poses major challenges to medicine as healthcare costs rise. Recently, faecal microbiota transplantation (FMT) has been discussed as a novel and effective method to decolonize MDRO. We compared the efficacy of different FMT methods to optimize the success rate of decolonization in patients with MDRO carriage.

Methods

In this prospective cohort study, we enrolled patients with MDRO carriages from 2018 to 2021. Patients underwent FMT via one of the following methods: oral capsule, oesophagogastroduodenoscopy (EGD), colonoscopy, or gastric tube. Successful decolonization of MDRO was defined as two consecutive negative results in stool cultures at least 1 week apart. Recolonization was defined as a positive stool culture result for CPE or VRE in a patient who had once been classified as having been decolonized. The primary endpoint was MDRO decolonization after each FMT modality. The secondary endpoint was the comparison of alpha and beta diversity of samples before and after FMT in different modalities.

Results

A total of 57 patients underwent FMT for MDRO decolonization. The colonoscopy group required the shortest time for decolonization, whereas the EGD group required the longest (24.9 vs 190.4 days, p = 0.022). The decolonization rate was highest in the EGD group (85.7%) and lowest in the gastric tube group (50.5%). The decolonization rate of the oral capsule group was comparable to that of the EGD group (84.6% vs 85.7%, p = 0.730). The important clinical factor associated with decolonization failure was antibiotic use after FMT (odds ratio = 6.810, p = 0.008). All four groups showed reduced proportions of MDRO species in the microbiome analysis after FMT.

Table 1. Baseline characteristics of patients with various methods of faecal microbiota transplantation (FMT)

Characteristics	Total
No. of participant	57
Age, years	65.0 (52.5–75.0)
Male, No. (%)	34 (59.6)
BMI (kg/m^2)	21.1 ± 3.7
Charlson Comorbidity Index score	2.3 ± 1.86
Duration of MDRO colonisation (days)	41.0 (17.5–100.5)
MDRO carriage	
VRE	24 (42.1)
CPE	12 (21.1)
MIX (VRE and CPE)	21 (36.8)
Antibiotics use before FMT within 1 week	25 (43.9)
Antibiotics use after FMT within 1 week	30 (52.6)
Laboratory test at FMT	
WBC count, 10^3/μL	7,312.1 ± 2,806.0
Haemoglobin, g/dL	10.9 ± 1.7
Platelet count, 10^3/μL	261.9 ± 105.3
BUN, mg/dL	19.0 ± 13.6
Creatinine, mg/dL	1.1 ± 1.2
AST, IU/L	35.4 ± 31.5
ALT, IU/L	23.4 ± 15.9
Total cholesterol, mg/dL	159.7 ± 55.0
Fasting glucose, mg/dL	111.2 ± 35.7
C-reactive protein, mg/dL	13.1 ± 12.0
Decolonisation rate No. (%)	36 (69.2)
Recolonisation rate No. (%)	11(19.3)

Data are expressed as number (percent), average ± standard deviation, or median (25–75%)
FMT, faecal microbiota transplantation; BMI, body mass index; MDRO, multidrug-resistant organism;VRE, vancomycin-resistant enterococci; CPE, carbapenemase-producing Enterobacteriaceae; WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate transaminase; ALT, alanine transaminase; LDL, low-density lipoprotein

Table 2. Comparison of study participants with different FMT modalities

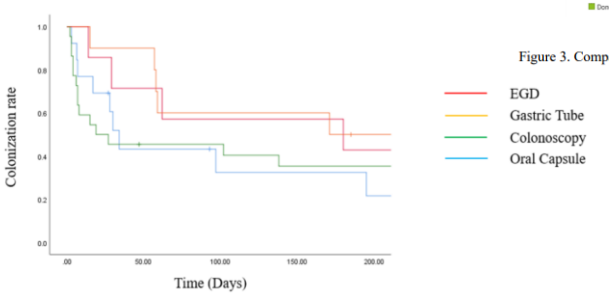
	Total	Oral capsule	EGD	Colonoscopy	Gastric tube	*p*-value[a]
No. of participant	57	14	9	23	11	
Age, years	65.0 (52.5–75.0)	75.5 (57.8–84.0)	72.0 (32.5–77.0)	63.0 (57.0–71.0)	66.0 (51.0–71.0)	0.494
Male, No. (%)	34 (59.6)	5 (35.7)	6 (66.7)	16 (69.6)	7 (63.6)	0.232
BMI (kg/m^2)	21.1 ± 3.7	21.5 ± 4.0	20.7 ± 4.1	20.9 ± 3.6	21.4 ± 3.4	0.952
Charlson Comorbidity Index score	2.3 ± 1.86	3.4 ± 2.0	1.6 ± 1.6	2.3 ± 1.9	1.6 ± 1.4	0.069
Duration of MDRO colonisation (days)	41.0 (17.5–100.5)	19.5 (8.0–116.0)	43.0 (23.0–138.5)	38.0 (21.0–82.0)	76.0 (27.0–273.0)	0.233
MDRO carriage						
VRE	24 (42.1)	2 (14.3)†‡	7 (77.8)*	12 (52.2)	3 (27.3)	**0.010**
CPE	12 (21.1)	3 (21.4)	2 (22.2)	4 (17.4)	3 (27.3)	0.966
MIX (VRE and CPE)	21 (36.8)	9 (64.3)†‡	0 (0)§	7 (30.4)	5 (45.5)	**0.010**
Antibiotics use before FMT within 1 week	25 (43.9)	7 (28.0)	2 (8.0)	11 (44.0)	5 (20.0)	0.574
Antibiotics use after FMT within 1 week	30 (52.6)	9 (30.0)	2 (6.7)	11 (36.7)	8 (26.7)	0.111
Laboratory test at FMT						
WBC count/μL	7,312.1± 2,806.0	7,211.4 ± 2,272.3	6,833.6 ± 2,325.1	6,804.3 ± 2,510.2	8,849.1 ± 3,978.2	0.513
Haemoglobin, g/dL	10.9 ± 1.7	10.7 ± 1.5	10.6 ± 1.3	11.5 ± 1.5	10.3 ± 2.4	0.217
Platelet count, 10^3/μL	261.9±105.3	247.7 ± 96.6	343.3 ± 166.5	249.9 ± 89.7	238.5 ± 54.3	0.323
BUN, mg/dL	19.0 ± 13.6	20.4 ± 14.5	17.1 ± 11.7	16.2 ± 9.4	24.7 ± 19.8	0.613
Creatinine, mg/dL	1.1 ± 1.2	1.6 ± 1.8	0.8 ± 0.7	0.8 ± 0.8	1.0 ± 1.1	0.248
AST, IU/L	35.4 ± 31.5	23.3 ± 22.1	51.8 ± 46.0	32.4 ± 25.9	43.9 ± 35.0	0.137
ALT, IU/L	23.4 ± 15.9	11.8 ± 6.4§	24.7 ± 18.1	25.3 ± 13.6	33.0 ± 19.8*	**0.005**
Total cholesterol, mg/dL	159.7 ± 55.0	164.9 ± 61.6	162.1 ± 48.5	152.2 ± 53.9	167.0 ± 59.0	0.532
Fasting glucose, mg/dL	111.2 ± 35.7	118.6 ± 38.2	100.0 ± 16.5	114.7 ± 44.2	103.7 ± 20.9	0.701
C-reactive protein, mg/dL	13.1 ± 12.0	10.3 ± 7.9	17.0 ± 16.5	13.3 ± 12.4	13.2 ± 12.2	0.915
Time to decolonisation	77.4 ± 107.1	75.8 ± 107.1	190.4 ± 158.3‡	24.9 ± 39.4†	90.8 ± 69.7	**0.005**
Decolonisation rate No. (%)	36 (69.2)	11 (84.6)	6 (85.7)	14 (63.6)	5 (50.0)	0.251
Recolonisation rate No. (%)	11 (19.3)	4 (28.6)	1 (11.1)	4 (17.4)	2 (18.2)	0.876

Data are expressed as number (percent), average ± standard deviation, or median (25–75%)
FMT, faecal microbiota transplantation; BMI, body mass index; MDRO, multidrug-resistant organism; VRE, vancomycin-resistant enterococci; CPE, carbapenemase-producing Enterobacteriaceae; WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate transaminase; ALT, alanine transaminase; LDL, low-density lipoprotein
[a]p-values are calculated using analysis of variance with Bonferroni method
*p < 0.05 vs. oral capsule; †p < 0.05 vs. EGD; ‡p < 0.05 vs. colonoscopy, §p < 0.05 vs. gastric tube

Table 3. Clinical variables associated with MDRO decolonisation failure after FMT

Baseline characteristic	OR (95% CI)	*p*-value
Age	1.005 (0.968–1.044)	0.789
Male	1.968 (0.568–6.824)	0.286
BMI	0.857 (0.718–1.024)	0.090
Underlying medical conditions		
Diabetes mellitus	0.804 (0.229–2.827)	0.734
Congestive heart failure	0.840 (0.251–2.816)	0.778
COPD	2.667 (0.574–12.396)	0.211
Chronic kidney disease	1.591 (0.426–5.939)	0.490
Charlson comorbidity score	1.014 (0.738–1.395)	0.930
Duration of MDRO colonisation (days)	1.001 (0.999–1.003)	0.177
MDRO carriage		
VRE	Reference	
CPE	0.254 (0.027–2.407)	0.232
MIX (VRE and CPE)	1.662 (0.466–5.932)	0.434
Antibiotics usage 1 week before FMT	2.275 (0.686–7.546)	0.179
Antibiotics usage 1 week after FMT	6.810 (1.641–28.257)	**0.008**
FMT modality		
Oral capsule	Reference	
EGD	0.917 (0.068–12.322)	0.948
Colonoscopy	3.143 (0.552–17.890)	0.197
Gastric tube	5.500 (0.782–38.698)	0.087

p-values with statistical significance is shown in bold text.
BMI; body mass index, COPD; chronic obstructive pulmonary disease, EGD; oendogastroduodenoscopy, CPE; carbapenemase-producing Enterobacteriaceae, MDRO; multi-drug-resistant organism, VRE; vancomycin-resistant enterococci



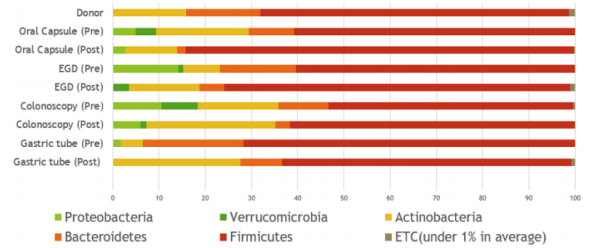


Figure 2. Composition changes in pre and post FMT of different modalities in the phylum level

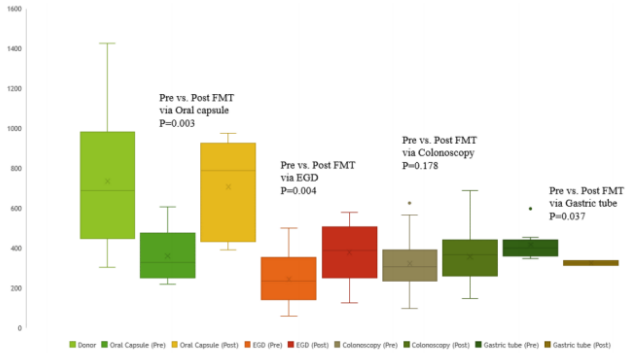


Figure 3. Comparison of ACE index of taxonomic data with different FMT modalities

Conclusion

Oral capsule is an effective FMT method for patients who can tolerate an oral diet compared to other conventional methods. Discontinuation of antibiotics after FMT is a key factor in the success of decolonization.