

Attitudes and preferences toward fecal microbiota transplantation among patients with cancer

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Research article

Keywords: Attitude and preference, fecal microbiota transplantation, influence factor, cancer patients

Posted Date: April 21st, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-23402/v1>

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Abstract

Background: To investigate the attitudes and preferences toward fecal microbiota transplantation (FMT) among patients with cancer, during anti-tumor treatment in the hospital.

Methods: A self-report questionnaire was administered to survey 101 patients with cancer at the Cancer Center of West China Hospital during their hospitalization and treatment. The patients were asked about their willingness to undergo FMT, and their preferences and attitudes regarding the donor, route, expenditure, and possible adverse effects.

Results: Most of the patients were willing to accept FMT. Patients with younger adults (OR = 0.92, 95% CI = 0.853-0.985, $P = 0.018$), a higher educational level (OR, 0.24; 95% CI, 0.101-0.576; $P = 0.001$) and later tumor stage (OR, 0.18; 95% CI, 0.058-0.568; $P = 0.003$) were more likely to select FMT as a treatment option. PS score was one of the most important factors that affecting the patients' choice of donor for FMT ($\chi^2 = 8.69$, $P = 0.013$), willingness to pay for FMT ($\chi^2 = 13.02$, $P = 0.005$), and concerns about adverse effects for FMT ($\chi^2 = 12.18$, $P = 0.002$).

Conclusions: Clinical characteristics of patients with cancer may influence whether they choose FMT as therapy, and if willing, attitudes regarding donor, route, expenditure, and adverse effects. Nurses and other healthcare providers should assess the demographic and clinical characteristics of patients with cancer to help them make appropriate medical decisions.

Introduction

Cancer is the second leading cause of death worldwide, and a major global public health problem [1]. Cancer is also the most burdensome disease in China, with steady increases in incidence and mortality since the year 2000, even as the population has rapidly aged and the economy has transformed.

Fecal microbiota transplantation (FMT) involves the transfer of a microbiome sample from the gut of a healthy donor to that of a patient, to restore a stable microbial gut community [2]. It is commonly used in the treatment of intestinal diseases such as pseudomembranous enterocolitis, inflammatory bowel disease, or irritable bowel syndrome, or infection by *Clostridium difficile*.

FMT has also been applied for the treatment of tumors, autoimmune diseases, metabolic diseases, and others. In various cancers, the gut microbiome modulates the efficacy of immunotherapy [3–4], radiotherapy [5], and chemotherapy [6]. Because the gut microbiome has a role in the development of tumors and efficacy of treatment, we believe that FMT may eventually constitute a novel anti-tumor strategy. While probiotic products can transitorily alter the functional bacterial species in the feces of most patients [7–8], the doses of probiotics given orally are much lower than the volume of the gut microbiome. Furthermore, during *ex vivo* cultivation the microorganisms in probiotic formulations lose some of their functions [9]. FMT overcomes these limitations.

FMT was first reported by the famous Chinese doctor Ge Hong, 1700 years ago, in his well-known book of traditional Chinese medicine, “Zhou Hou Bei Ji Fang” [10]. The fecal suspension was referred to as “yellow soup” and was effective for the treatment of severe diarrhea and oral food poisoning [10]. However, the aesthetics of the modern patient regarding this treatment often differs from that of the ancient. Developing criteria, guidelines, and a standardized method for FMT administration requires the consideration of patients’ attitudes and preferences.

This study determined the willingness of patients with cancer to undergo FMT as an anti-tumor treatment in the hospital, and investigated the factors that influence their attitudes and preferences.

Methods

Sample and setting

The criteria for inclusion in this study were: diagnosed with cancer by pathology; aged ≥ 18 years; survival time ≥ 3 months; an understanding of the disease progress; and able to read and write Chinese. Patients with any of the following were excluded: critical condition; cognitive impairment or psychiatric illness; or failure to complete the questionnaire, leading to missing data.

Of 120 patients with cancer admitted to the project from 1 September 1 2018 to 30 September 30 2018 at West China Hospital of Sichuan University, the final population comprised 101 (84.2%). Of 19 patients who failed to complete the interview or questionnaire, 15 were not interested in our study, and 4 were not able to read and write Chinese.

Instrument

A questionnaire was designed to assess the patients’ attitudes and preferences regarding FMT. The questionnaire consisted of 15 questions which were based on previous studies [11–14]. Ten questions were used to collect demographic data and clinical indexes such as gender, age, education, health insurance, religion, tumor stage, and performance status (PS). Five questions gathered information regarding attitudes and preferences toward the FMT option, and the donor, route, expenditure, and potential adverse effects.

In the attitudes and preferences section of the questionnaire, patients answered the following open-ended questions:

■ Are you willing to receive fecal microbiota transplantation?

If no, please choose the reasons:

worry about side effects worry about efficacy financial burden

the therapy disgusts me other, please specify ____

If yes, please answer the following questions:

■ Who do you prefer to be the donor, and why?

relative friend stranger reason ____

■ Which method of delivery do you prefer, and why?

oral nasoduodenal tube colonoscopy reason ____

■ What is the highest expense you are willing to pay for this treatment, and why?

≤10K 10-20K 20-30K ≥30K reason ____

■ Which adverse event is most worrisome, and why?

flatulence infection diarrhea fatigue reason ____

Design and data collection

A cross-sectional survey was conducted of patients with cancer via convenience sampling in a cancer center of China. A semi-structured interview was developed to collect data. The Ethics Committee of the West China Hospital granted approval for the study. Before the formal investigation began, the patients' primary care physicians were contacted to gain their support, and a clinical nurse was trained to interview the participants. A specified room was prepared for the interview.

The nurse used a printed questionnaire collect data from the participants. All the participants were given the same instructions for the study and were asked not to share their responses with other participants. The interviewer recorded each participant's responses to the questions, without any attempt to influence their answers. The data were analyzed by an independent statistician who was not involved in the data collection or storage. All the data was confidential, and available only for reasons that were in accordance with the goal of the study.

Statistical analysis

The demographics and clinical characteristics of the participants were analyzed statistically. The Kruskal-Wallis test was used to find significant differences in the answers to the questionnaire according to participants' demographics and clinical characteristics. Binary logistic regression analysis was used to identify which of the factors were associated with the patients' willingness to undergo FMT. SPSS statistic software (version 18.0) was employed to analysis the data. A 2-sided P value < 0.05 was considered statistically significant.

Results

Sample characteristics

Table 1 provides a description of the sampled characteristics. One hundred and one patients with cancer participated in the study, with a mean age of 53.6 years (20–81 y). Among them, 47 (46.5%) were male, 77 (76.2%) were married, and 82 (81.2%) lived with family members. Eight (7.9%) belonged to an ethnic minority, 55 (54.4%) had completed some college, and 12 (11.9%) were religious. Financially, 91 (88.1%) owned health insurance, and the annual incomes of 67 (66.4%) were less than ¥100K. The tumor stages of 99 (98.0%) participants were from I to IV. Performance status scores were 2, 1, and 0 for 8 (7.9%), 12 (11.9%), and 80 (80.2%) patients, respectively.

Table 1
 Characteristics of 101 study subjects

Characteristic		<i>n</i> (%)
Age	18–40	23(22.8)
	41–60	58 (57.4)
	≥ 61	20 (19.8)
Gender	Men	47(46.5)
	Women	54 (53.5)
Nation	Han	93 (92.1)
	Minority	8 (7.9)
Religion	Yes	12 (11.9)
	No	89 (88.1)
Health insurance	Governmental health insurance	56 (55.4)
	Commercial health insurance	33 (32.7)
	Self-paying	12 (11.9)
Marital status	Married	77 (76.2)
	Divorced	14 (13.9)
	Widows	10 (9.9)
Living situation	With family members	82 (81.2)
	Live alone	19 (18.8)
Education level	Middle school or lower	29 (28.7)
	High school	17 (16.9)
	Some college	18 (17.8)
	Undergraduate or higher	37 (36.6)
Primary tumor site	Head and neck cancer	37 (36.6)
	Abdominal cancer	20 (19.8)
	Thoracic cancer	44 (43.6)
Income (annual)	≤ 10 k	19 (18.8)
	10–50 k	24 (23.8)

Characteristic		<i>n</i> (%)
	50–100 k	24 (23.8)
	≥ 100 k	34 (33.6)
Tumor stage	0	2 (2.0)
	1	37 (36.6)
	2	25 (24.8)
	3	37 (36.6)
Performance status score	0	81 (80.2)
	1	12 (11.9)
	2	8 (7.9)

Willingness to undergo FMT

Of the 101 participants interviewed, 91.1% (92 of 101) were willing to choose FMT, and 8.9% (9 of 101) were not. The binary logistic regression analysis revealed that patients with the following characteristics were more likely to choose FMT in their treatment (Table 2): younger patients (OR = 0.92, 95% CI = 0.853–0.985, $P = 0.018$); higher educational level (OR = 2.82, 95% CI = 1.321–6.027, $P = 0.007$); and later tumor stage (OR = 2.53, 95% CI = 1.044–6.121, $P = 0.040$). Factors which were not associated with the willingness to accept FMT were: gender; ethnicity; religion; health insurance; marital status; living with family members; primary tumor site; income; or PS score.

Table 2
Binary logistic regression model for factors associated with willingness toward FMT

Factor	<i>B</i>	<i>SE</i>	<i>Wals</i>	<i>OR</i>	<i>95% CI</i>	<i>P</i>
Age	-0.087	0.037	5.597	0.917	0.853–0.985	0.018
Education level	1.037	0.387	7.178	2.822	1.321–6.027	0.007
Tumor stage	0.927	0.451	4.221	2.527	1.044–6.121	0.040

Preferred donor

The Kruskal-Wallis test indicated that the main factors affecting the patients' choice of donor for FMT included PS score ($\chi^2 = 8.69$, $P = 0.013$; Table 3). Patients with lower PS scores were more likely to prefer the stool of a relative.

Table 3
Kruskal-Wallis test for factors associated with donor toward FMT

Characteristic	relative	friend	stranger	χ^2	<i>P</i>
Performance status score	0	52	1	19	
	1	6	2	4	
	2	2	0	6	8.69 0.013

FMT route of delivery

The factors that influenced the patients' preference of FMT delivery route were gender ($\chi^2 = 11.25$, $P = 0.004$; Table 4). Female gender were each associated with a preference for oral delivery.

Table 4
Kruskal-Wallis test for factors associated with routes toward FMT

Characteristic		take orally	nasoduodenal tube	colonoscopy	χ^2	<i>P</i>
Gender	Male	31	8	5		
	Female	46	2	0	11.25	0.004

Expenditure for FMT

The Kruskal-Wallis test showed that the main factors affecting patients' willingness to pay for FMT were: having health insurance ($\chi^2 = 15.15$, $P = 0.002$); income ($\chi^2 = 10.48$, $P = 0.015$); PS score ($\chi^2 = 13.02$, $P = 0.005$) and tumor stage ($\chi^2 = 23.29$, $P = 0.000$; Table 5). The respondents who had to self-pay, with an annual income less than ¥50,000, with PS 1 and 2, or with tumor stage III or IV, were more likely to spend no more than ¥20,000 on the FMT.

Table 5
Kruskal-Wallis test for factors associated with expenditure toward FMT

Characteristic		≤ 10K	10-20K	20-30K	≥ 30K	χ^2	<i>P</i>
Health insurance	Governmental health insurance	13	12	12	14	15.15	0.002
	Commercial health insurance	21	5	0	5		
	Self-paying	5	4	1	0		
Income (annual)	≤ 10 k	9	2	3	3	10.48	0.015
	10–50 k	14	3	1	0		
	50–100 k	7	12	0	5		
	≥ 100 k	9	4	9	11		
Performance status score	0	31	11	11	19	13.02	0.005
	1	3	7	2	0		
	2	5	3	0	0		
Tumor stage	□	1	0	0	0	23.29	0.000
	□	6	2	11	14		
	□	11	11	1	0		
	□	21	8	1	5		

Influence of potential adverse effects

The single factor analysis indicated that the factors that influenced concerns about adverse effects during FMT treatment were health insurance ($\chi^2 = 8.03$, $P = 0.018$), and PS score ($\chi^2 = 12.18$, $P = 0.002$; Table 6). The patients without religion or governmental health insurance, or a nil PS score, were more likely to worry about serious adverse effects such as emesis and diarrhea.

Table 6
Kruskal-Wallis test for factors associated with adverse effect toward FMT

Characteristic		flatulence	infection	diarrhea	fatigue	χ^2	<i>P</i>
Health insurance	Governmental health insurance	4	5	10	32	11.21	0.011
	Commercial health insurance	3	4	12	12		
	Self-paying	4	2	3	1		
Performance status score	0	3	10	22	37	16.04	0.001
	1	7	0	1	4		
	2	1	1	2	4		

Discussion

Willingness toward FMT

Popular opinion regarding FMT suffers from prejudice against feces and aesthetic concerns, which could limit it as a treatment option in cancer. However, a long-term follow-up study on colonoscopic fecal microbiota transplant found that 97% of patients infected with *Clostridium difficile* preferred FMT to antibiotics [13]. Jalanka et al. [14] reported that 97.6% of the patients treated with FMT were willing to choose FMT as first-line treatment over antibiotics for recurrent *C. difficile* infection. The present study is in accord with these results, in which 91.1% of these patients with cancer were willing to include FMT in a multi-strategy treatment program. Of the 9 patients who were not willing to accept FMT therapy, 4 and 2 worried about efficacy and side effects, respectively, 2 had a financial burden, and 1 believed that FMT was disgusting.

Zipursky et al. [11] reported that respondents were more likely to choose FMT if it was recommended by their physician, and there was no association with level of education. This is inconsistent with our research, in which the patients most likely to accept FMT had a higher educational level or late tumor stage. Of note, the population's educational level in the present study (28.7% of the patients had not completed high school) was much higher than that of the Zipursky et al. [11] study (2.7%). Additional studies are needed to determine which method of administration is most acceptable to patients.

Preferred donor

FMT donors have included spouses, first-degree relatives, other family members, friends or partners, and strangers to the patients [14]. In the present study, 65.2% of the patients preferred spouses and relatives as donors, while 31.5% chose a stranger. Only 3 (3.3%) patients wanted a friend or partner as a donor.

The percentage of patients who chose a stranger as donor increased with patients' PS score. These patients considered the issue of donor source comprehensively and rationally, and accepted that FMT provided a benefit, regardless of donor. Of note, for many diseases the effectiveness of FMT does not depend on the relationship between the recipient and donor. Yet, when treating diseases related to heredity or environment, spouses and relatives should be avoided [15].

FMT route of delivery

Many FMT routes involve the upper, middle, and lower gut [16–18]. These include retention enema, nasogastric tube, colonoscopy, gastroscopy, and esophagogastroduodenoscopy [19]. The methods most commonly used are retention enema and colonoscopy. A systematic review showed that FMT delivered via retention enema or colonoscopy for recurrent infection of *Clostridium difficile* was more effective than either gastroscopy or nasoenteric tube [20]. According to the present research, most of the patients wanted to receive FMT by oral capsule; most of them believed that the capsule was easier and more convenient than other FMT routes. Future FMT standards of delivery should respect the patients' preference, if it is as safe and effective as other routes.

Expenditure toward FMT

There is no consensus regarding the most cost-effective route for FMT. A recent study found that FMT via colonoscopy was the most cost-effective strategy against infection by *Clostridium difficile* [21–22]. Yet, another study indicated that the most cost-effective route was enema [23]. In the present study, 39 (42.4%) patients were willing to undergo FMT therapy only if the cost was less than ¥10,000. Only 19 (20.7%) patients would pay more than ¥30,000. China's average per capita disposable income in 2018 was ¥28,228 [24]. Thus, therapy that costs more than ¥30,000 is expensive for most people in China. Emilie et al. [23] found that patients in France with recurrent community-onset infection due to *Clostridium difficile* were willing to pay €32,000/QALY (quality-adjusted life-year) for FMT via enema. In the present study, taken together, patients who had tumor stage \geq , governmental health insurance, with PS 0, and more than ¥100,000 in annual income were willing spend more than ¥20,000 on FMT.

Influence of potential adverse effects

There have been a few adverse events attributed to FMT in previous studies. Transient adverse responses were observed after FMT, including mild diarrhea, pain, fever, fatigue, and exhaustion [9, 25], but no additional studies have reported complications or adverse events [26–27]. It may be that, in the future, specific complications will be associated with particular methods of administration of FMT, but FMT appears to be a safe therapy with few serious adverse effects. The present results suggest that for ~ 50% of patients, fatigue was the most concerning adverse reaction; although fatigue plagues the lives of most patients with cancer.

Limitations

This study has some limitations. First, the sample size was small. Second, this is a cross sectional investigation based on a single center. Together, these factors suggest that there may be a selective bias

in the research, and we should be cautious with the interpretation of results and conclusions. However, this is the first study of the attitudes and preferences toward FMT among patients with cancer, and the results warrant a further clinical multicenter survey with a larger sample. Finally, the use of a self-report questionnaire in this study may limit the generalizability of the results.

Conclusion

The purpose of this study was to investigate the attitudes and preferences toward FMT among patients with cancer during anti-tumor treatment in the hospital. The preliminary evidence is that characteristics of patients with cancer may influence whether they choose FMT as therapy, and if willing, attitudes regarding donor, route, expenditure, and adverse effects. Oncology nurses and other members of the healthcare team should assess the background and clinical characteristics of patients with cancer, to help them make appropriate medical decisions. This will improve the quality of life for patients with cancer, and even prolong their overall survival.

Declarations

Ethics approval and consent to participate

The Ethics Committee of West China Hospital of Sichuan University approved the study. All procedures performed in the study were conducted in accordance with the 1964 Helsinki Declaration. Informed consent was obtained from every patient.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study were anonymized, with its supplementary information files (Additional file 1).

Competing interests

The authors declare that they have no competing interests.

Funding

This study was conducted with funding from Sichuan University West China Nursing Discipline Development Special Fund Project (HXHL 19028). The funding agency had no role in the study design, collection of data, data analysis, or writing of this manuscript.

Authors' contributions

Study design: RZ, CY, JL. Data collection: ZY, QX, LC. Statistical analysis: LC. Manuscript writing: RZ, YF, JZ. All authors read and approved the final manuscript.

Acknowledgments

The authors thank all the patients and the clinical team of the Cancer Center at the West China Hospital of Sichuan University.

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