Efficacy of fecal microbiota transplantation in a patient with chronic intractable constipation

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Key Clinical Message
We have presented the first case report of FMT therapy for a patient with chronic intractable constipation. This therapy resulted in good, medium-term outcomes. Follow-up analysis of the intestinal flora suggested that transplanted microbes from the donor, particularly Bifidobacterium and Clostridium cluster IX, may have been incorporated into the recipient.

KEYWORDS
chronic intractable constipation, fecal microbiota transplantation, intestinal microbiota, short chain fatty acids (SCFAs), terminal fragment length polymorphism (T-RFLP) method

1 | INTRODUCTION
Fecal microbiota transplantation (FMT) therapy for patients with Clostridium difficile infection colitis has been found to have surprising efficacy.1 Dysbiosis of the intestinal flora is a problem and possible cause in diseases such as colorectal carcinoma, hepatocellular carcinoma, diabetes mellitus, obesity, and NASH.2–5 In addition, dietary habits strongly affect the intestinal flora. Many patients have chronic constipation, and although these patients take laxatives and pre- and probiotics to improve their intestinal flora, the success of these approaches is limited. We used FMT therapy for a patient with chronic intractable constipation and achieved significant short- and medium-term efficacy. This is the first case report of FMT therapy for such a patient.

2 | CASE HISTORY/EXAMINATION
The patient was an 83-year-old male who had suffered with chronic intractable constipation for over fifty years. He had been treated with many anti-constipation agents and probiotics, including magnesium oxide, carmellose sodium, D-sorbitol, sodium picosulfate hydrate, and yogurt containing Lactobacillus gasseri, but the frequency of defecation remained at 7-10 days and the stool volume was small, with a Bristle Stool Score (BSS) of 1 for classification of fecal properties. Based on an abdominal X-ray, feces accumulated in the intestines, resulting in a very firm abdomen and anorexia. A general examination indicated that the patient had a mild Alzheimer’s type of dementia that caused forgetfulness in daily life.
nephew, were first examined (Figure 1 and Table 1). We confirmed the validity of the donor based on several infectious disease tests and the results of intestinal flora analysis. Also, the donor gave a guarantee to provide feces for transplant. The analysis of the patient’s intestinal flora showed a depletion of both *Bifidobacterium* and some short chain fatty acids (SCFAs), especially acetic acid, propionic acid, and butyric acid (Table 2). The intestinal flora was analyzed by a terminal fragment length polymorphism (T-RFLP) method after DNA extraction from feces.\(^6\),\(^7\) The concentrations of seven SCFAs in the fecal samples were measured by gas chromatography-mass spectrometry.\(^8\) The transplant-microbial solution was prepared from the donor’s feces,\(^1\) and then about 400 mL was infused into the recipient by colonoscopy. The solution was infused into the cecum to the ascending colon only once. FMT therapy was performed at Fukushima Daiichi Hospital.

### 4 | OUTCOME AND FOLLOW-UP

Immediately after FMT therapy, the recipient defecated every day and developed abdominal distensions without the need for drug therapy. The fecal properties and bowel movements are summarized in Table 3. The efficacy of the FMT therapy was remarkable and continued for 1 month. An examination of the patient’s intestinal flora at 1 month after FMT therapy showed that the composition resembled that of the donor, with a notable increase in the populations of *Bifidobacterium* and *Clostridium* cluster IX in the recipient (Figure 1 and Table 1). The patient’s dementia symptoms of forgetfulness also showed a minor improvement after FMT therapy. The positive effects of FMT therapy on normal bowel movements, frequent passage, and normal fecal properties were still present after more than 11 months.

### 5 | DISCUSSION

Bowel movements are accelerated by SCFAs such as butyric acid and propionic acid,\(^8\) and SCFAs\(^9\) are generated by *Bifidobacterium, Lactobacillus*, various types of *clostridium* clusters, and intestinal flora in general. Incorporation of transplanted microbes after FMT therapy has not been reported, but the results from our follow-up examination suggested that *Bifidobacterium* and *Clostridium* cluster IX were incorporated into the recipient’s intestinal flora. This beneficial effect of FMT therapy may be applicable for other diseases, such as diabetes mellitus, inflammatory bowel disease, and dementia. We plan to perform a full analysis of the incorporated microbes in a further study.

### 6 | CONCLUSIONS

We have presented the first case report of FMT therapy for a patient with chronic intractable constipation. This therapy resulted in good short- and medium-term outcomes. Follow-up analysis of the intestinal flora suggested that transplanted microbes from the donor, particularly *Bifidobacterium* and *Clostridium* cluster IX, may have been incorporated into the recipient’s intestinal flora analyzed by T-RFLP method. It may be a possibility that the further follow-up observation and the detailed full analysis of microbes in this case lead to the new developments of FMT treatment.
**Table 1** Classification groups analyzed by terminal fragment length polymorphism in donor and recipient microbiota

| OUT | Classification group (%) | Donor | Recipient (before FMT) | Recipient (1 month after FMT) |
|-----|---------------------------|-------|------------------------|-------------------------------|
| 106 | *Clostridium* subcluster XIVa | 0.0   | 0.0                    | 0.0                           |
| 110 | *Clostridium* cluster IX    | 13.9  | 0.0                    | 33.6                          |
| 124 | *Bifidobacterium*           | 10.8  | 0.0                    | 8.8                           |
| 137 | *Prevotella*                | 0.0   | 0.0                    | 0.0                           |
| 168 | *Clostridium* cluster IV    | 0.0   | 0.0                    | 0.0                           |
| 317 | *Prevotella*                | 33.4  | 6.3                    | 12.3                          |
| 332 | *Lactobacillus* order       | 1.2   | 1.4                    | 2.5                           |
| 338 | *Clostridium* cluster       | 0.5   | 1.1                    | 1.4                           |
| 366 | *Bacteroides*               | 9.9   | 6.3                    | 6.2                           |
| 369 | *Clostridium* cluster IV    | 0.0   | 1.7                    | 0.0                           |
| 423 | *Clostridium* cluster X VIII| 0.0   | 0.0                    | 0.0                           |
| 443 | None                       | 0.0   | 0.6                    | 0.0                           |
| 469 | *Bacteroides*               | 5.7   | 37.6                   | 14.2                          |
| 494 | *Clostridium* subcluster XIVa| 1.8  | 3.6                    | 3.8                           |
| 505 | *Clostridium* subcluster XIVa| 0.0  | 0.0                    | 0.0                           |
| 517 | *Clostridium* subcluster XIVa| 0.0  | 0.0                    | 0.0                           |
| 520 | *Lactobacillus* order       | 0.0   | 5.0                    | 0.0                           |
| 641 | None                       | 0.0   | 0.0                    | 0.0                           |
| 650 | *Clostridium* cluster XVIII  | 0.9   | 0.9                    | 0.0                           |
| 657 | *Lactobacillus* order       | 1.6   | 17.9                   | 7.1                           |
| 749 | *Clostridium* cluster IV    | 6.1   | 0.4                    | 1.4                           |
| 754 | *Clostridium* subcluster XIVa| 1.2  | 1.8                    | 0.6                           |
| 770 | None                       | 0.9   | 0.7                    | 0.0                           |
| 853 | *Bacteroides*               | 1.8   | 1.6                    | 0.0                           |
| 919 | *Clostridium* cluster IX    | 2.2   | 4.6                    | 3.6                           |
| 940 | *Clostridium* subcluster    | 2.6   | 2.7                    | 1.4                           |
| 955 | *Clostridium* subcluster XIVa| 1.8  | 1.0                    | 0.0                           |
| 968 | None                       | 0.5   | 0.8                    | 0.0                           |
| 990 | *Clostridium* subcluster XIVa| 3.2  | 3.8                    | 3.1                           |

OUT indicates operational taxonomic unit.

**Table 2** Production of short chain fatty acids

| SCFA            | Donor | Recipient (before FMT) |
|-----------------|-------|------------------------|
| Acetic acid     | 57.2  | 31.5                   |
| Propionic acid  | 23.3  | 4.9                    |
| Butyric acid    | 14.4  | 4.4                    |
| Isobutyric acid | 0.6   | 1.6                    |
| Valeric acid    | 2.3   | 1.0                    |
| Isovaleric acid | 0.7   | 2.0                    |
| Caproic acid    | 1.0   |                        |

Data are shown as concentrations (μmol/g). A blank indicates a value lower than the limit of detection (LOD). The LODs for acetic acid, propionic acid and butyric acid were 2.0, 0.7 and 0.7 μmol/g, respectively. The LODs for isobutyric acid, valeric acid, isovaleric acid and caproic acid were all 0.3 μmol/g.

**Table 3** Changes of fecal properties and bowel movements in the recipient before and after FMT therapy

| Item                        | Before FMT | After FMT |
|-----------------------------|------------|-----------|
| Abdominal distension        | Marked     | None      |
| Borborygmus feeling         | Almost nothing | Almost normal |
| Use of laxative             | Many laxatives | None    |
| Feces frequency             | 0-1/week   | 1/day     |
| Feces weight                | Minimum    | Moderate  |
| Feces odor                  | Offensive  | Mild      |
| Feces color                 | Blackish-brown | Yellowish-brown |
| Bristol Stool Scale         | 1          | 3-4       |
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CONFLICT OF INTEREST

The authors declare that they have no other competing interests.

AUTHOR CONTRIBUTIONS

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