Fecal Transplantation using a Nasoenteric Tube during an Initial Episode of Severe Clostridium difficile Infection

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The incidence of Clostridium difficile infection is increasing worldwide, and its severity and resulting mortality are also on the rise. Metronidazole and oral vancomycin remain the treatments of choice, but there are concerns about treatment failure and the appearance of resistant strains. Furthermore, antibiotic therapy results in recurrence rates of at least 20%. Fecal transplantation may be a feasible treatment option for recurrent C. difficile infection; moreover, it may be an early treatment option for severe C. difficile infection. We report a case of severe C. difficile infection treated with fecal transplantation using a nasoenteric tube during an initial episode. This is the first reported case of fecal transplantation using a nasoenteric tube during an initial episode of C. difficile infection in Korea.

Key Words: Fecal transplantation; Fecal microbiota; Clostridium difficile; Nasoenteric tube

Introduction

The incidence, severity, and resulting mortality of Clostridium difficile infection are increasing worldwide [1-3]. In spite of the considerable increase in the incidence and severity of C. difficile infection, metronidazole and oral vancomycin remain the treatments of choice [4]. Metronidazole is generally used for mild and moderate C. difficile infection, but treatment failure is a growing problem. Vancomycin is costly, and there is concern about the appearance of resistant strains [5]. Furthermore, antibiotic therapy has recurrence rates of at least 20%, which increase with each subsequent C. difficile infection [6]. Els van Nood et al. reported that in patients with recurrent C. difficile infection, fecal transplantation resulted in better treatment outcomes compared with conventional antibiotic treatment. Fecal transplantation had a cure rate of 81.3% following a single nasoenteric infusion and 93.8% following a second infusion, while standard vancomycin therapy with or without...
bowel lavage had a 23.1-30.8% cure rate [7]. Fecal transplantation may be a treatment option for recurrent *C. difficile* infection; moreover, it may be an early treatment option for severe *C. difficile* infection [8]. In Korea, two cases of severe refractory *C. difficile* infection treated with fecal transplantation during an initial episode have been reported. One case used esophagogastroduodenoscopy (EGD) while the other case used enema [9, 10]. Here, we report the first case of severe initial *C. difficile* infection, refractory to antibiotics, that was treated with fecal transplantation using a nasoenteric tube in Korea.

**Case Report**

A 65-year-old man visited the emergency room with a 3-day history of bilateral leg weakness and fever. His blood pressure was 86/43 mmHg, and his body temperature was 39.3°C at presentation. He had a history of hypertension and recent surgery for lumbar spinal stenosis three months before admission. Initial peripheral blood count showed a white blood cell count of 4,710/mm$^3$ (neutrophils, 92.2%; lymphocytes, 5.2%; monocytes, 1.4%), hemoglobin level of 11.3 g/dL and platelet count of 137,000/mm$^3$. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were 13.2 sec and 34.8 sec, respectively, and C-reactive protein level was 286.06 mg/L. Blood chemistry showed a total protein level of 5.1 g/dL, albumin level of 2.9 g/dL, total bilirubin level of 0.5 mg/dL, aspartate aminotransferase/alanine aminotransferase 27/17 IU/L, BUN/Cr 56.6/2.42 mg/dL, Na/K 138/4.1 mEq/L and Ca/P 7.6/2.7 mg/dL. Lumbar magnetic resonance imaging (MRI) was performed and revealed infective spondylitis and multiple paraspinal abscesses. The patient received empiric intravenous antibiotic treatment with 2.0 g ceftriaxone every 24 hours and 200 mg teicoplanin every 24 hours after peripheral blood culture and urine culture. He underwent incision and drainage of multiple abscesses. *Streptococcus intermedius* was identified in all three initial blood cultures, and the minimal inhibitory concentration (MIC) for penicillin G was 0.016 µg/mL. Antibiotics were changed to 4 million units penicillin G every 4 hours. On the 35th hospital day, he had urinary tract infection and bacteremia from an extended-spectrum beta-lactamase (ESBL) organism and was treated with 500 mg imipenem every 6 hours.

On the 59th hospital day, during conservative treatment for infective spondylitis, the patient developed a fever of 38.1°C and diarrhea; his blood pressure was 89/58 mmHg. Due to suspicion of *C. difficile* infection, oral 500 mg metronidazole was given every 8 hours empirically. Stool *C. difficile* toxin A/B and culture were confirmed to be positive. On the 60th hospital day, laboratory results revealed a white blood cell count of 39,560/mm$^3$ (neutrophils, 89.4%; lymphocytes, 6.2%; monocytes, 2.8%), hemoglobin level of 11.8 g/dL, platelet count of 292,000/mm$^3$, BUN/Cr of 18.0/0.65 mg/dL, and albumin level of 1.8 g/dL. On the 61st hospital day, oral metronidazole was switched to 250 mg oral vancomycin every 6 hours due to increased severity of diarrhea and the detection of paralytic ileus on abdominal X-ray despite administration of oral metronidazole. Intravenous metronidazole (every 8 hours) and vancomycin enema 500 mg (every 6 hours) were also added to the treatment course. Unfortunately, symptoms did not improve, and disseminated intravascular coagulation (DIC) progressed although leukocytosis was improved. On the 74th hospital day, laboratory results showed a white blood cell

![Figure 1](image-url)
count of 3,240/mm$^3$ (neutrophils, 71.0%; lymphocytes, 20.1%; monocytes, 6.8%), a hemoglobin level of 7.8 g/dL, platelet count of 67,000/mm$^3$, PT/aPTT of 22.6 sec/65.4 sec, albumin level of 1.9 g/dL and C-reactive protein level of 77.2 mg/L. Fe-cal transplantation was recommended and the patient consented to the procedure. The patient’s wife, who had no relevant medical history and no symptoms of acute disease, was selected as the donor. On the 75th hospital day, fecal transplantation was performed. The tip of a nasoenteric tube was placed in the third portion of the duodenum by EGD. Fifty grams of stool collected from the donor was diluted with 500 mL normal saline and the supernatant was filtered out with gauze. This solution was placed into the feeding bag and infused through a nasoenteric tube for 30 minutes (Fig. 1).

After fecal transplantation, diarrhea and ileus gradually improved and fever subsided. Platelet count, PT/aPTT and albumin level were also improved (Fig. 2). On the 84th hospital day, 9 days after fecal transplantation, laboratory test results were as follows: white blood cell count 6,280/mm$^3$ (neutrophils, 65.3%; lymphocytes, 24.2%; monocytes, 5.3%), hemoglo-

**Table 1. Cases of fecal transplantation in Korea**

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Indication</th>
<th>Sex</th>
<th>Age</th>
<th>Donor relationship</th>
<th>Infusion route</th>
<th>Infusion volume</th>
<th>Outcome</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gweon et al. 2013 [9]</td>
<td>Refractory CDI</td>
<td>Male</td>
<td>83</td>
<td>Wife</td>
<td>EGD</td>
<td>Stool 150 g, Normal saline 300 mL</td>
<td>CDI resolved</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Recurrent CDI</td>
<td>Male</td>
<td>86</td>
<td>Daughter</td>
<td>EGD</td>
<td>Stool 100 g, Normal saline 300 mL</td>
<td>CDI resolved</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Moon et al. 2013 [10]</td>
<td>Recurrent CDI</td>
<td>Male</td>
<td>83</td>
<td>Daughter</td>
<td>Enema</td>
<td>Stool 50 mL, Normal saline 200 mL</td>
<td>CDI resolved</td>
<td>Mild diarrhea</td>
</tr>
<tr>
<td></td>
<td>Refractory CDI</td>
<td>Female</td>
<td>70</td>
<td>Son</td>
<td>Enema</td>
<td>Stool 50 mL, Normal saline 300 mL</td>
<td>CDI resolved</td>
<td>None</td>
</tr>
<tr>
<td>This case</td>
<td>Refractory CDI</td>
<td>Male</td>
<td>65</td>
<td>Wife</td>
<td>Nasoenteric tube</td>
<td>Stool 50 g, Normal saline 500 mL</td>
<td>CDI resolved</td>
<td>None</td>
</tr>
</tbody>
</table>

CDI, Clostridium difficile infection; EGD, esophagogastroduodenoscopy.
> 60 years, serum albumin < 2.5mg/dL, body temperature > 38.3°C, or a white blood cell count > 15,000/mm³ within 48 hours of diagnosis; or if they met one of the following criteria: endoscopic evidence of pseudomembranous colitis or treatment in the intensive care unit for C. difficile infection. Refractory infection was defined as non-resolution of C. difficile infection despite 7 days of therapy with oral vancomycin. The cure rate was 79% (11 of 14). This study included six patients with initial episodes of C. difficile infection [13]. Because of its cost effectiveness, high cure rate, minimal risk and reestablishment of normal flora, fecal transplantation has even been proposed as the initial treatment modality for severe C. difficile infection [14].

In Korea, four cases of fecal transplantation have been reported (Table 1). Two cases were recurrent C. difficile infections, and the other two cases were refractory C. difficile infections. Two cases used EGD and infused stool via the biopsy channel of EGD. The other two cases used enema. In all four cases, C. difficile infection resolved. Two patients had adverse events. One patient who received EGD experienced vomiting, and another patient who received enema had mild diarrhea after fecal transplantation. In our case, we used a nasogastric tube placed in the third portion of the duodenum by EGD to perform the fecal transplantation. The patient had no adverse events and recovered from C. difficile infection.

Fecal transplantation can be performed using a nasogastric tube, nasoenteric tube, EGD, colonoscopy, flexible sigmoidoscopy, or enema [12]. Two review studies compared fecal transplantation outcomes based on the route of administration of donor feces. One systematic review reported that fecal transplantation by EGD and nasoenteric tube had a lower resolution rate than that by colonoscopy and enema (76.4% vs > 88.7%). Most patients received treatment or preparation before fecal transplantation; therefore, estimating the effect of fecal transplantation alone was difficult [15]. The other review study compared colonoscopic fecal transplantation with nasogastric fecal transplantation from 12 published studies. Colonoscopic fecal transplantation had a superior resolution rate (93.2%) compared with nasogastric fecal transplantation (85.3%), but the difference was statistically nonsignificant [16]. There has been no randomized, controlled trial comparing outcomes based upon the route of administration of fecal transplantation. Further investigation is required to determine which route of administration is best.

Some adverse events were reported. Transient GI symptoms are common, including decreased bowel movement, abdominal cramping, increased bowel sounds and abdominal discomfort. In fecal transplantation via the upper gastrointestinal tract, the risks of aspiration and vomiting should be considered. The colonoscopic approach could be dangerous in patients with severe colitis or colonic distension [12]. A randomized controlled study by Els van Nood et al. reported acute adverse events including diarrhea (94%), cramping (31%) and belching (19%) in nasoenteric infusion, but these symptoms improved within 3 hours [7]. Long-term adverse events are not well known and require further investigation [8].

This case had one major limitation. Generally, oral vancomycin is stopped before fecal transplantation; however, oral vancomycin was continued and tapered in our case due to concerns regarding the potential failure of fecal transplantation. This could make it difficult to estimate the effect of fecal transplantation alone. Nevertheless, we are confident that fecal transplantation resulted in the resolution of C. difficile infection because the patient exhibited no improvement during the previous 14 days of oral vancomycin therapy, but recovered dramatically after fecal transplantation.

In conclusion, fecal transplantation could be a viable treatment option not only for recurrent C. difficile infection, but also for severe initial infection. Further investigation is required to establish the optimal method of fecal transplantation and to ensure long-term safety.

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