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Efficacy of fecal microbiota transplant in conjunction with oral vancomycin for the treatment of recurrent Clostridium difficile

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ABSTRACT

Objective: To determine the effectiveness of fecal microbiota transplant in addition to traditional therapy of oral vancomycin for the treatment of recurrent *Clostridium difficile* infections. **Methods:** Google Scholar was searched to identify randomized control trials using the terms vancomycin, fecal transplant, *c. diff*, and recurrent. **Results:** Three studies met inclusion criteria and two found a statistically significant benefit to the addition of fecal microbiota transplant to vancomycin therapy. Cammarota, et al. reported a 90% cure rate when administering fecal microbiota transplant in addition to vancomycin as opposed to a 26% cure rate with vancomycin alone with a P value of 0.0001.[3] Hvas, et al. found a 71% clearance rate with dual therapy and 19% cure rate with antibiotics alone at a P value of 0.001.[4] Hota, et al. showed that only 43.8% of patients had clearance with a 56.2% recurrence rate.[5] **Conclusion:** This review offered conflicting evidence in regards to the efficacy of fecal microbiota transplants in reducing *Clostridium difficile* recurrence. Differing variables including study location, administration route, antibiotic duration, and follow up period doesn't allow for a definitive recommendation at this time. Further research using larger sample sizes and congruent vancomycin regimens are crucial to better evaluate this intervention.

INTRODUCTION

Clostridium difficile (*C. difficile*) has been notoriously associated with a high infection and mortality rate in the United States. According to the Centers for Disease Control and Prevention (CDC), *C. difficile* was responsible for 450,000 gastrointestinal infections and resulted in 29,300 deaths in 2011. This accounted for 12.1% of all health-care associated infections, showing a high rate of hospital associated morbidity.[1] *Clostridium difficile* is a Gram-positive anaerobic bacillus that commonly causes intestinal pathology secondary to the production of exotoxins. In a young and healthy individual, the presence of *C. difficile* is well controlled by the gut's natural flora, thus simply considered colonization. These individuals may test positive for *C. difficile* in their stool, but present asymptomatically. However, in an individual receiving excessive broad-spectrum antibiotic therapy, the normal flora is reduced to levels where *C. difficile* is able to proliferate and the body is unable to adequately keep the growth in check. This is classified as a *C. difficile* infection and the patient will have symptoms including numerous watery stools, fever, nausea, and abdominal pain. The diagnosis of *C.*

difficile is commonly made through a combination of symptomatology and fecal sampling. Polymerase chain reaction (PCR) assays are utilized to detect the toxin B gene associated with the infection. Alternative testing measures include enzyme immunoassays (EIA) that detect toxin A, toxin B, or both. Stool culturing is also acceptable due to its high sensitivity, but may lead to a high rate of false-positives due to non-toxigenic strains of the bacteria.[1]

The most widely accepted recommendation for the treatment of recurrent *C. difficile* infection is pulse-tapered oral vancomycin taken for a duration of 2 to 8 weeks.[2] Fecal microbiota transplant (FMT) is an emerging adjuvant therapy for those with episodes of recurrent *C. difficile* infection previously treated with antibiotic therapy. The purpose of FMT is for reintroduction of normal gut flora in an effort to restore the intestinal environment to a state where *C. difficile* is unable to proliferate. This is accomplished via a stool sample from a healthy donor administered via colonoscopy, enema, nasojejunal tube, or orally by capsule.[2] The objective is to determine whether the addition of FMT to an oral vancomycin taper is superior to the taper alone when treating a patient with recurrent *C. difficile.*

PICO

Population: Male and female patients 18 years or older with recurrent *Clostridium difficile* colitis infections
Intervention: Fecal microbiota transplant (via nasojejunal and rectal administration) plus oral vancomycin
Control: Oral vancomycin
Outcome: Decreased recurrence of subsequent *Clostridium difficile* colitis infections

CLINICAL QUESTION

Among male and female patients 18 years or older with recurrent *Clostridium difficile* colitis infections, are fecal microbiota transplants plus oral vancomycin more effective than oral vancomycin alone in decreasing the recurrence of subsequent *C. difficile* colitis infections 2-4 months post-treatment?

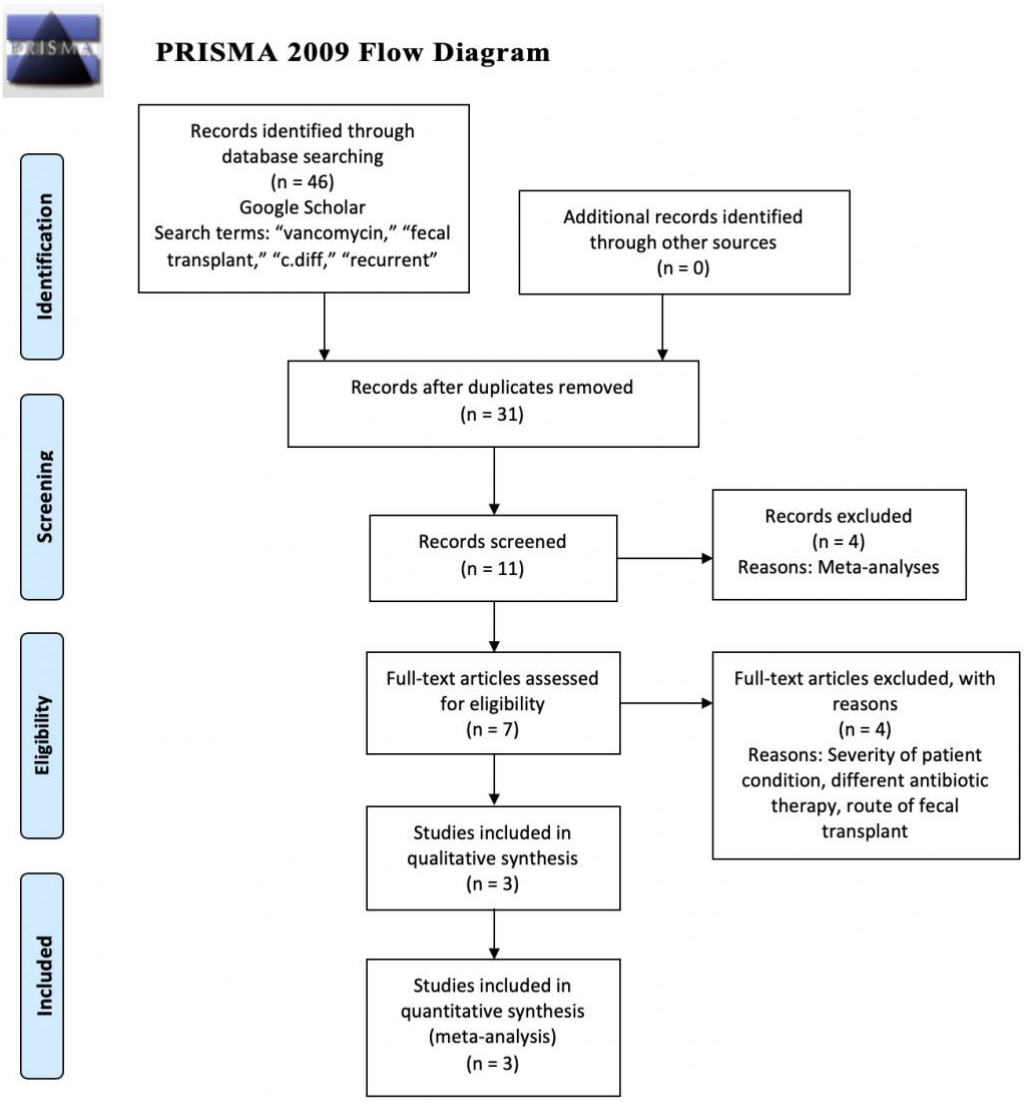

Figure 1: PRISMA flow diagram

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

METHODS

In September 2018, the Google Scholar database was searched using the terms: "vancomycin," "fecal transplant," "c.diff," and "recurrent." This search produced 46 articles in total, fifteen of which were duplicates and thus removed from the collection. Of these articles, eleven were screened and four were removed because they were meta-analysis. At this point, seven full-text articles were assessed for eligibility. Of those, four were removed due to the high severity of the

patient population, differing antibiotic therapy, and differing route of fecal transplant administration. This left three articles that met all of the necessary criteria which included: *Fecal Microbiota Transplantation Is Superior to Fidaxomicin for Treatment of Recurrent Clostridium difficile Infection. Hvas et al.; Oral Vancomycin Followed by Fecal Transplantation Versus Tapering Oral Vancomycin Treatment for Recurrent Clostridium difficile Infection: An Open-Label, Randomized Controlled Trial. Hota, et al.;* and *Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent Clostridium difficile infection. Cammarota, et al.* Figure 1 outlines the process of article screening used by the authors.

RESULTS

Study #1

Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent Clostridium difficile infection. Cammarota et. al.[3]

Study Objective: To determine the efficacy of single or repeated colonoscopic FMTs on recurrent *Clostridium difficile* infection (CDI) compared to standard oral vancomycin therapy.

Study Design: This study was an open-label randomized control trial (RCT) due to the difficulty of concealing the interventions. The subjects were from A. Gemelli University Hospital in Rome, Italy and were subject to the inclusion and exclusion criteria seen in Table 1. In order to be considered a CDI, the individual must have had a positive fecal test of the *C. difficile* toxin with 10 weeks of previous antibiotic use, and diarrhea (loose or watery stools $\geq$3/day or $\geq$8 loose stools in the last 2 days). Participants were randomized into one of two groups, those treated with the standard vancomycin regimen or FMT. The vancomycin group took 125mg of the antibiotic

"by mouth four times daily for 10 days, followed by a pulse regimen (125– 500mg/day every 2–3 days) for at least 3 weeks."[3] The FMT group took 125mg of oral vancomycin four times/day for 3 days with an oral bowel prep on the last day or two of antibiotic therapy before the fecal infusion via colonoscopy. If there was recurrent CDI after the initial fecal transplant (FT), subsequent FTs were performed in three day increments until remission was achieved. This schedule can be better visualized in Figure 2. It is important to note that the first two patients of the FT group differed from this protocol in that FT was repeated every 10 days if there was recurrence of CDI instead of every three days. The protocol was refined to its latter form after the authors of the study decided that FT every 10 days was not frequent enough.

The majority of fecal donors for this study were related (16/20) to the recipients and the stool was collected on the same day as the infusion. The stool was mixed with 500mL of normal saline and infused via colonoscopy into the large intestine, ensuring coverage of the entire colon including proximal segments such as the cecum and the ascending colon. After infusion, the patients were kept in the right lateral recumbency position for one hour to ensure retention of the transplant in the proximal aspects of the colon.

Follow-up for the study extended out to 10 weeks from the end of the intervention (10 weeks from the end of vancomycin, or 10 weeks from the last FMT depending on which group). The primary endpoint was no recurrence of CDI within the 10-week period. Recurrence was defined as unexplainable diarrhea (loose or watery stools $\geq$3/day for 2 days or $\geq$8 loose stools for 2 days) regardless of *C. difficile* toxin test results. The secondary endpoint was cure, defined as the absence of diarrhea for the 10 weeks with two negative fecal *C. difficile* toxin tests. Patients were followed closely for the first week and told to keep a stool diary. They were then followed

weekly during weeks 2–10 of the research. Fecal testing for *C. difficile* toxin was performed on weeks 5 and 10 and if an episode of diarrhea occurred at any point.

Table 1. Inclusion and Exclusion Criteria for Study 1.[3]	
Inclusion Criteria	Exclusion Criteria
1. ≥18 years of age 2. ≥3-month life expectancy 3. Recurrent CDI after antibiotic treatment (≥10 days of vancomycin 125 mg four times daily or ≥10 days of metronidazole 500 mg three times a day)	1. Immunocompromised 2. Pregnancy 3. Antibiotic use other than vancomycin, fidaxomicin, or metronidazole 4. Have other potential causes of diarrhea 5. In the intensive care unit 6. Unable to undergo colonoscopy

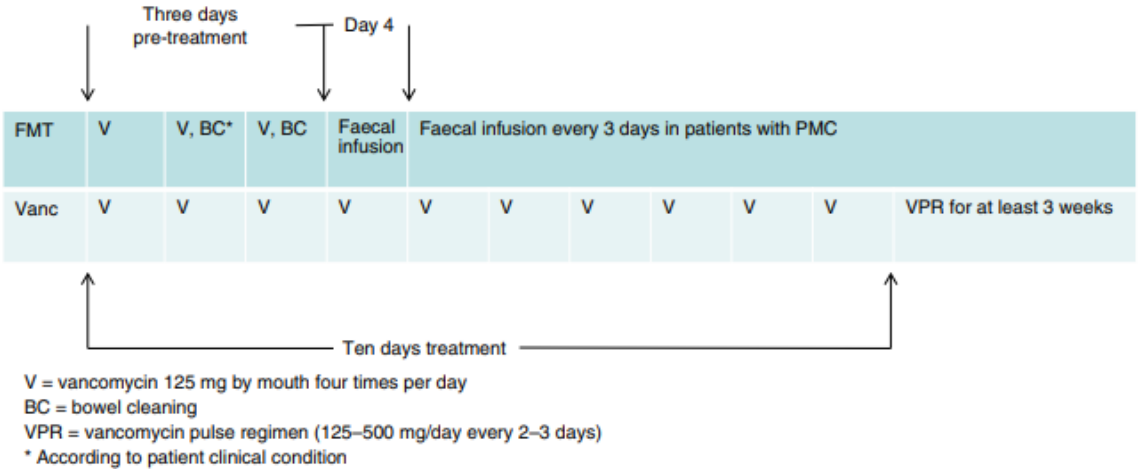

Figure 2. Timeline of therapies[3]

Results: Of the 20 patients assigned the FMT group, 13 were cured with a single FT. At the end of the 10-week period and subsequent fecal infusions, 18 of 20 (90%) were considered cured as specified by the criteria in the section above. The vancomycin group had a cure rate of only 26% (5 of 19) and recurrence rate of 74% (14 out of 19). With both intention-to-treat and per-protocol analysis, FMT was shown to be drastically more effective at achieving lasting remission (90% vs 26%, p=0.0001) as compared to standard vancomycin therapy. The number needed to treat

(NNT) was calculated to be 1.56. This means that about 2 patients must be treated with FMT in order to see additional benefit as opposed to vancomycin alone.

Critique: Strengths of the study were the duration of the trial and well as repeated stool samples to test for *C. difficile*. The study also had extremely statistically significant results and a thorough follow-up plan with the patients. One potential critique is that there was no blinding for the study. Additionally, it is unknown if repeated bowel preps could have caused a diminished amount of diarrhea following the preps due to complete evacuation of the bowel (potentially skewing the results) or if it had some effect itself on diluting/clearing out *C. difficile* in the bowel. The location of the study was also a concern as such a small sample size located only in Rome could allow for geographical and dietary differences that would prevent this study from being applicable outside of that region. The majority of the fecal donors in this study were related to the recipients. This is a crucial consideration when interpreting the results but it is unclear as to if relatedness would be of benefit or detriment in regards to the clearance of infection.

Study #2

Fecal Microbiota Transplantation Is Superior to Fidaxomicin for Treatment of Recurrent Clostridium difficile Infection. Hvas et al.[4]

Study Objective: To compare the efficacy of combination treatment of FMT with vancomycin to that of fidaxomicin or vancomycin alone for the resolution of *Clostridium difficile* infection 8 weeks after treatment.

Study Design: This study was an open-label single-center RCT that took place from April 5, 2016 through June 10, 2018. The subjects were patients of a gastroenterology clinic in Denmark

whom had a history of recurrent *C. difficile* infections (rCDI). Of 120 patients initially referred for study participation, 64 were selected based on the inclusion and exclusion criteria outlined below in Table 2. The study group had a median of 4 previous CDI infections and the median age was 68 years. They were randomized into one of the three following groups: FMT preceded by 4-10 days of vancomycin 125 mg four times daily (QID), 10 days of treatment with fidoxamicin 200 mg two times daily (BID), or 10 days of treatment with vancomycin 125 mg QID. The combination treatment group had 24 participants, the fidaxomicin alone group had 24 participants, and the vancomycin alone group had 16 participants. Notably, the patients who experienced rCDI following the primary allocated treatment or were too ill to be included in the study were offered rescue fecal microbiota transplants. Although this study looked at two types of antibiotic therapy, vancomycin and fidaxomicin, this systematic review focused on vancomycin specifically in the treatment of *C. difficile* infections.

FMT was administered via colonoscopy or nasojejunal tube and the method of delivery was decided based on patient preference. Frozen-thawed single-donor solutions of 50 g were administered. The donors were recruited and screened at a public blood center located in Aarhus University Hospital in Aarhus, Denmark. All donors were healthy individuals and samples were obtained on a strictly voluntary basis. Those that selected the colonoscopy route of administration received a standard lavage prior to the FMT with the dose divided in thirds and given in the terminal ileum, cecum, and anally to the hepatic flecture. The nasojejunal route was given over 10 minutes with the patient upright following an overnight fast. In general, the researchers advocated for the colonoscopy as there were historically higher success rates with this method and the nasojejunal option being reserved for those that could not tolerate the procedure.

The primary end point of this study was "combined clinical resolution and a negative CD test result without the need for rescue FMT/vancomycin (FMTv) or colectomy 8 weeks after the initial treatment."[4] The CD test included a GeneXpert PCR that targeted genes for toxin A and B, binary toxin, or CD ribotype 027. A positive result consisted of any combination of the toxins of interest. Those participants that had a positive CD test and clinical recurrence before the 8-week time frame were offered FMTv.

Table 2. Inclusion and Exclusion Criteria for Study 2.[4]

Inclusion Criteria	Exclusion Criteria
1. Recurrent *C. difficile* infection 2. ≥18 years of age 3. At least 3 or more liquid stools (Bristol 6-7) per day 4. Positive polymerase chain reaction test result for *C. difficile* toxin A, toxin B, or binary toxin 5. At least 1 prior treatment course with vancomycin or fidaxomicin for *C. difficile* infection	1. Pregnancy or breastfeeding 2. Inability to speak or understand the Danish language 3. Ongoing antibiotic treatment 4. Use of drugs with a known interaction with vancomycin or fidaxomicin 5. Allergy to vancomycin or fidaxomicin 6. Fulminant colitis that contraindicated medical treatment 7. Treating physician's evaluation that the patient could not tolerate project inclusion a. Frail or septic patient

Results: The primary outcome of a negative CD test and clinical resolution was achieved in 17 of the 24 (71%) of those that received FMT/vancomycin, 8 of the 24 (33%) with fidaxomicin, and 3 of 16 (19%) of those who received vancomycin alone. All statistical calculations were made using a 95% confidence interval. The overall result of the study showed that FMT, delivered by nasojejunal tube or colonoscopy, after a short course of vancomycin was superior to either fidaxomicin or vancomycin alone. Importantly, 24 of the study participants enrolled had a positive CD test and clinical relapse before the 8 weeks was reached. They were given rescue FMT/vancomycin and remained in the study. Following the rescue treatment, 20 of the 24

individuals met the primary outcome of a negative CD test and clinical resolution at the end of 8 weeks.

When investigating potential reasons for FMT treatment failure, the researchers discovered that hemoglobin was the "strongest and only statistically significant covariate associated with failure of FMT."[4] The calculated odds ratio was 0.5 with a 95% confidence interval per point increase in hemoglobin. An odds ratio of less than one means that there are lower odds of FMT failure with every one point increase in the hemoglobin level. The mean hemoglobin in those that failed FMT treatment was 6.7 mmol/L in women and 6.0 mmol/L in men. Those that were successful with FMT treatment showed a mean level of 7.3 mmol/L in women and 7.9 mmol/L in men. Overall, the presence of anemia was shown to have a 6.3 times greater risk of failure of FMT. The NNT for this study was 1.92.

Critique: This particular study was novel in that it claims to be the first clinical trial to compare the efficacy of fidaxomicin with that of FMT in the treatment of recurrent *C. difficile* infections. It was also the first time that the potential link between anemia and prediction of successful FMT for the treatment of this issue was discussed, but needs further validation in future research. The largest strength of this study was the statistically significant result of the FMT/vancomycin group having a much higher rate of clearance and thereby lower rate of recurrence than the other antibiotics alone with a P value of 0.001. In addition, their careful selection of patient population allowed for the least amount of variability between groups.

A weakness of this study was that 15 participants (23%) had concomitant inflammatory bowel disease which may have affected the resolution results. Another weakness was that the study utilized six different donor samples for the FMT. While this may have been difficult to

avoid, the difference between samples may have contributed to a more effective or less effective result. Furthermore, the researchers included the data of those that required a rescue FMT/vancomycin treatment during the 8-week course with those that only received one treatment. None of the patients included in the study tested positive for CD ribotype 027 which means that these results may not be applicable to that patient population. Finally, the study was unblinded meaning that observer bias may have had an effect on the reporting of results.

Study #3

Oral Vancomycin Followed by Fecal Transplantation Versus Tapering Oral Vancomycin Treatment for Recurrent Clostridium difficile Infection: An Open-Label, Randomized Controlled Trial. Hota. et. al.[5]

Study Objective: To determine if fecal microbiota transplant following 14 days of vancomycin treatment was more efficacious compared to a six-week taper of vancomycin alone in preventing recurrence of *Clostridium difficile* Infection (CDI).

Study Design: This study was a phase II/III open-label randomized control trial (RCT) performed in Ontario, Canada. Inclusion and exclusion criteria for the study are expressed in Table 3. Participants were randomized with a 1:1 ratio to either the fecal transplant (FT) group or the vancomycin taper group. The fecal transplant group consisted of oral vancomycin at 125 mg every 6 hours for 14 days followed by a one-time FT via enema 48 hours after the vancomycin was discontinued. The vancomycin taper group had the same regimen for the first 14 days, but instead of FT, they received "vancomycin 125 mg orally every 12 hours for 1 week; then, vancomycin 125 mg orally every 24 hours for 1 week; then, vancomycin 125 mg orally every second day for 1 week; then, vancomycin 125 mg orally every third day for 1 week."[5]

The FT group was assigned a particular stool donor and all of the enemas consisted of feces less than 48 hours old. Eleven of the 16 donors were related to their recipient and the stools were examined microscopically to ensure microbiota diversity. 50 grams of donor feces were liquified into 500 mL of normal saline and administered via enema over the course of 10-30 minutes. Both groups were monitored for recurrence for 120 days post-completion of the initial shared two-week vancomycin treatment. Thus day 0 for the FT and vancomycin taper groups were the days the FT was given and when the 4-week vancomycin taper was started respectively. Stool samples were collected from both groups at study visits on days 7 and 120 to test for *Clostridium difficile* using either PCR for *C. difficile* toxin gene or enzymatic immunoassay (EIA) for *C. difficile* toxin. Additional stool samples were submitted if diarrhea occurred before the end of the 120-day observation period. There were also four phone appointments at days 4, 21, 42, and 84 to further assess for recurrent CDI and side effects from the therapies. The primary endpoint of the study was recurrence of confirmed, symptomatic CDI.

Table 3. Inclusion and Exclusion Criteria for Study 3.[5]

Inclusion Criteria	Exclusion Criteria
1. ≥ 18 years of age 2. Confirmed history of ≥ 2 CDIs via a. Polymerase chain reaction (PCR) for *C. difficile* toxin gene OR b. Enzymatic immunoassay (EIA) for *C. difficile* toxin 3. Received oral vancomycin to treat at least 1 past CDI (minimum of 500mg/day for 10 days)	1. Neutropenia 2. Severely immunocompromised or Graft-vs-host disease 3. Fulminant CDI 4. Inability to take oral vancomycin 5. Gastrointestinal diseases that may be associated with diarrhea 6. Elective surgery with use of perioperative antibiotics or interventions such as chemotherapy within 120 days 7. Pregnancy 8. Bleeding disorder

Results: Initially, 30 patients met inclusion and exclusion criteria and 16 were randomly assigned to the FT group and 14 to the vancomycin taper. Of note, only 12 individuals were actually assigned to the vancomycin taper because two patients were excluded from the study (one for being non-compliant and one for wanting FT at another facility). At the conclusion of the study, 9 of the 16 patients (56.2%) assigned to the FT experienced recurrence, correlating with 43.8% of patients with cleared symptoms for 120 days. The vancomycin taper had 5 of 12 patients (41.7%) experience recurrence, correlating with 58.3% clearance. Recurrence of CDI occurred on average 9 days after treatment with FT and 7 days after finishing the vancomycin taper (35 days after initially starting the vancomycin taper). Although the FT group had a higher rate of recurrence and similar symptoms as the vancomycin taper in days 0-7, symptoms were reported as less severe by the patients in the FT group on days 7-14. Abdominal pain, abdominal bloating, and foul-smelling stools were reported in 36.4%, 27.3%, and 27.3% of FT patients respectively in days 7-14. The vancomycin group had rates of 75%, 58.3%, and 50% in regards to the occurrence of the three most common symptoms listed above. Donor relatedness and the recurrence of CDI in the FT group were found to have no correlation. The NNT for this RCT was unattainable.

Critique: A weakness of the RCT was that it was not blinded, thus potentially resulting in confirmation bias and skewed subjective reporting. Another weakness was the small sample size thereby giving the study less power. Additionally, intention-to-treat analysis was not used because of the relatively large proportion of the vancomycin taper group that was excluded, and instead per protocol analysis was utilized. This was the appropriate choice of analysis considering the nature of the two participants that did not complete the study. One was non-compliant and the other wished to receive treatment at another facility, leaving the analysis to

include only those that actually received treatment. Strengths of the study were its duration of follow-up and that both groups were treated equally in regards to follow-up appointments and post-intervention stool testing.

DISCUSSION

This review investigated the efficacy of the addition of FMT to the traditional therapy of vancomycin for the treatment of recurrent *C. difficile* infections. The three RCTs reviewed showed conflicting results regarding the usefulness of this intervention. Studies 1 and 2 show an advantage of combining FMT with some variation of vancomycin therapy for the treatment of recurrent CDI, while Study 3 shows the exact opposite. Study 3 claimed that FMT was not as effective as vancomycin taper which is in direct contradiction to the other results.

There were a couple of possible factors identified leading to these opposing results. Study 3 administered the FMT by enema only once, while Studies 1 & 2 gave the FT by colonoscopy and included repeat FTs if there was no immediate resolution or early recurrence of CDI. The colonoscopy allowed the transplant stool to reach higher up in the gastrointestinal tract thus allowing for better retention in the proximal colon. In addition, Study 1 ensured that the 500mL was spread across more intestine and the patient remained in the right lateral recumbency position following infusion, all allowing for better retention. In Study 3, only 10 of 16 patients could retain 80% of the enema. Therefore, a large amount of the FT via enema would be immediately defecated back out and decrease the therapeutic benefit. These factors could have negatively affected the FMT success rate in Study 3 and one should interpret their results with caution.

The authors from Study 3 also stated that the use of 14 days of oral vancomycin could have caused too much death of natural intestinal microflora and one FT was not enough to restore the symbiotic bacterial balance. In addition, "vancomycin was discontinued 48 hours prior to FT. Subsequent data demonstrate that vancomycin remains detectable in feces for 4–5 days after discontinuation of therapy, potentially impacting the microbiota of the FT."[5] Study 1 included a bowel prep which could have advantageously washed out any remaining vancomycin from the intestines to allow the FMT to adhere without interference, thus eliminating this factor. However, it is unclear if the bowel cleansing was effective secondary to washing out the *C. difficile* vegetations or residual vancomycin.

The variability in duration of antibiotic treatment prior to FMT between the three studies contributed a significant amount of heterogeneity. Study 3 administered vancomycin for 14 days, Study 2 for 4-10 days, and Study 1 for 3 days. This could result in variance of the amount of *C. difficile* present at the time of FMT administration.

The method of donor feces selection may have also impacted the differing results between studies. Studies 1 and 3 made an effort to use donor feces from relatives of the patients when possible resulting in 11 of the 16 and 16 of the 20 cases respectively. Study 2 gathered donations on a voluntary basis and made no mention of relation to the recipient. This could have heavily influenced the efficacy of the FMT as relatives potentially have similar diets and natural gut flora.

A large issue across all three studies was the small sample size. Study 3 had 28 participants, Study 2 had 64 participants, and Study 3 had 39 participants. Such small sample sizes increase the risk of Type II error thus decreasing the overall power of the results. It is important to keep in mind that this intervention focuses on a very specific population of those

with recurrent *C. difficile* infections and may be difficult to find numerous participants in one area. In addition, the concept of FMT may not be widely accepted by all and some patients that may qualify for the study could refuse due to the nature of the intervention. Another important similarity between studies was that all of them were conducted outside of the United States. It is unclear of the significance of this difference, but important to note as diets and gut flora in different countries may be different from that in America. One should apply the results of these studies with caution if practicing in the United States.

FMT was shown to be statistically more effective at achieving lasting remission in both Studies 1 and 2 as compared to standard vancomycin therapy with P values of 0.0001 and 0.001 respectively. Study 3 did not provide a P value for comparison. NNT were as follows: Study 1 was 1.56, Study 2 was 1.92, and Study 3 was unattainable. This shows that Studies 1 and 2 had more efficacious FMT protocols and thus future research should follow their procedure guidelines.

While the use of FMT has shown promising results in regards to the clearance of *C. difficile* infections, it does not come without risk. As noted in the study completed by Hota, et al., administration via colonoscopy lends the patient to an increased risk of bowel perforation that is otherwise minimized with oral antibiotic therapy. In addition, the study also showed an increased occurrence of acute fever, nausea, vomiting, abdominal pain, and smelly stools in the FMT group as compared to the vancomycin group.[5] It is imperative to consider these risks when selecting the patient population for this form of therapy as well as thorough education for the participant.

CONCLUSION

Fecal microbiota transplant is an emerging and increasingly researched therapy for the treatment of recurrent CDI. In examining the three randomized control trials above, there were many variables between the studies that caused difficulty in deciphering the data. Location, administration route, antibiotic duration, and follow up period among many other components varied for each of the three articles. However, with the summed results presented in the three studies, FMT is a promising adjuvant therapy when added to the standard vancomycin treatment. At current, adverse outcomes in the studies from FMT were mild and the potential for decreased recurrence has led the authors to recommend FMT for the potential long-term benefit. Additional studies with larger sample sizes and congruent vancomycin regimes will be needed to further quantify the benefits of fecal transplantation for the treatment of recurrent *C. difficile* infection.

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