High Rates of Cure and Long-Term Symptom Resolution with Both Capsule and Lower Gastrointestinal Fecal Microbiota Transplantation for Recurrent *Clostridium difficile* Infection

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Background

- Fecal microbiota transplantation (FMT) is the treatment of choice for recurrent *C. difficile* infection (CDI).
- Long-term and real-world outcomes are still unclear.
- Most studies report on average several weeks follow-up time.
- Best route of administration is still unclear:
  - **Colonoscopy (lower GI tract) vs Capsule (upper GI tract)**
    - FMT: makes a difference because capsule FMTs are much easier to perform and don’t involve the risk of a procedure.
    - Capsule FMT: patient only needs to come into the office and in one sitting swallows the 30 capsules.
    - Colonoscopy: scheduled procedure by GI involving sedation and prior bowel prep; risk of bleeding, infection, perforation.
- **Current thought** is that colonoscopy or lower GI tract FMT is preferred because it delivers the stool and “good bacteria” to the cecum, which is the area of bowel that C. difficile affects.
- But, recent RCT compared the two types of FMT and found them to be equal at 12 week follow-up1.
- Another single-center observational study reported better outcomes in colonoscopies than FMT via NG tube (upper GI tract) at 2 week follow-up2.

**Purpose:**
- To evaluate the long-term real-world outcomes of FMT at UCLA.
- To investigate if there is a difference in outcomes between lower GI tract FMT and capsule FMT.

Methods

- **Study Design:**
  - Online survey of all patients who received FMT for recurrent CDI at UCLA Health from 12/2014 through 9/2017.
  - Survey questions addressed: route of FMT (capsule vs lower GI tract), timing of improvement, recurrence of symptoms or CDI.
- **Majority of survey questions were from the NIH PROMIS** GI symptom scale to assess various GI symptoms in the week prior to FMT and the week prior to taking the survey (long-term follow-up).
- Categories of questions were: belly pain, constipation, diarrhea, fecal incontinence, gas & bloating, and nausea & vomiting.
- Chart review provided demographic information and time to follow-up.
- **Statistical Analysis:** Changes pre/post FMT were assessed using the Wilcoxon signed-rank test.

Results

**Survey Inclusion and Exclusion Work Flow:***

- Attempted to contact 88 possible participants.
- 68 persons were contacted & asked to complete survey.
- 27 persons did not start online survey.
- 4 persons partially completed online survey.

60 persons completed online survey & 5 persons completed survey via phone.

45 total participants.

**Outcomes:**

Comparing subjective severity of symptoms on a scale of 1 being the least to 5 being the most:

- Frequency of poor appetite
- Amount of days with diarrhea
- Frequency of feeling bloated
- Frequency of need to empty the bowels
- Bothersomeness of abdominal pain
- At its worst, severity of abdominal pain
- At its worst, severity of bloating
- Frequency of feeling nauseated

Comparing pre- and post-FMT symptoms in capsule vs lower GI tract FMTs:

**Comparing pre- and post-FMT symptoms overall:**

<table>
<thead>
<tr>
<th></th>
<th>Pre Median (IQR)</th>
<th>Post Median (IQR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of abdominal pain</td>
<td>4 (2-5)</td>
<td>1 (1-2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>At its worst, severity of abdominal pain</td>
<td>3 (2-4)</td>
<td>1 (1-2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Botherliness of abdominal pain</td>
<td>4 (2-5)</td>
<td>1 (1-2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Amount of days with diarrhea</td>
<td>5 (5-5)</td>
<td>2 (1-4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Botherliness of diarrhea</td>
<td>5 (4-5)</td>
<td>1 (1-3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Frequency of feeling need to empty bowels or else would have an accident</td>
<td>5 (4-5)</td>
<td>2 (1-3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Frequency of thinking would pass gas but instead have incontinence of stool</td>
<td>3 (2-4)</td>
<td>1 (1-2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Frequency of feeling bloated</td>
<td>4 (3-5)</td>
<td>2 (1-3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>At its worst, severity of bloating</td>
<td>3 (2-4)</td>
<td>1 (1-2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Frequency of feeling nauseated</td>
<td>4 (3-5)</td>
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<td>&lt;0.001</td>
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**Comparing subjective severity of symptoms in capsule vs lower GI tract FMTs:**

<table>
<thead>
<tr>
<th></th>
<th>Capsule (blue)</th>
<th>Lower GI tract (red)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of abdominal pain</td>
<td>3 (2-4)</td>
<td>5 (4-5)</td>
<td>0.001</td>
</tr>
<tr>
<td>At its worst, severity of abdominal pain</td>
<td>2 (1-3)</td>
<td>4 (2-5)</td>
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</tr>
<tr>
<td>Botherliness of abdominal pain</td>
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<td>0.001</td>
</tr>
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<td>0.001</td>
</tr>
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</table>

**Demographics:**

- **Age (range, average, SD):** 18-90 years, 61.2 years, SD 18.0.
- **Gender:** 66% (51/77) female.
- **Race:** 80% (62/77) Caucasian.

**Majority of survey questions were from the NIH PROMIS GI symptom scale to assess various GI symptoms in the week prior to FMT and the week prior to taking the survey (long-term follow-up).**

**Purpose:**

- To evaluate the long-term real-world outcomes of FMT at UCLA.
- To investigate if there is a difference in outcomes between lower GI tract FMT and capsule FMT.

**Conclusions:**

- FMT led to a high rate of long-term cure.
- There was a significant improvement in multiple GI symptoms months to years after transplant, regardless of route of administration.
- Route of FMT did not impact symptom relief.
- There was a significant improvement in multiple GI symptoms months to years after transplant, regardless of route of administration.

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References:

3. **Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children**. *2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)*. *Clinical Infectious Diseases*, 65(5), 713-782.