Efficacy of Fecal Microbiota Transplantation for Recurrent C. difficile Infection

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METHODS

A PubMed literature search was performed for studies involving FMT treatment for recurrent CDI. The following key words were used: Clostridium difficile, C. difficile, fecal microbiota transplantation, fecal bacteriotherapy, and vancomycin. Results were limited to RCT and systematic reviews of human subject studies written in English and available in full text. Eight articles were reviewed. The data extracted from these are listed in the table below.

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Design (Level of Evidence)</th>
<th>Patients</th>
<th>Outcome</th>
<th>Conclusion</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shrestha et al. 2015</td>
<td>Systematic review (IV)</td>
<td>13 studies, 260 patients for inclusion</td>
<td>35.7%</td>
<td>LTR 30% (IV)</td>
<td>Prevalence, limited by single-group design, no placebo group, small sample size, heterogeneity, statistical significance, potential selection bias, no reporting of complications, no reports of long-term follow up</td>
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<tr>
<td>Neuzil et al. 2015</td>
<td>Systematic review (IV)</td>
<td>11 studies, 214 patients for inclusion</td>
<td>73.9%</td>
<td>LTR 89% (IV)</td>
<td>Prevalence, limited by single-group design, no placebo group, small sample size, heterogeneity, statistical significance, potential selection bias, no reporting of complications, no reports of long-term follow up</td>
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<tr>
<td>Ammann et al. 2013</td>
<td>Systematic review (IV)</td>
<td>41 randomized trials, 1127 patients for inclusion</td>
<td>66.2%</td>
<td>LTR 89% (IV)</td>
<td>Prevalence, limited by single-group design, no placebo group, small sample size, heterogeneity, statistical significance, potential selection bias, no reporting of complications, no reports of long-term follow up</td>
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<tr>
<td>Riska et al. 2011</td>
<td>Systematic review (IV)</td>
<td>27 randomized trials, 1113 patients for inclusion</td>
<td>66.2%</td>
<td>LTR 89% (IV)</td>
<td>Prevalence, limited by single-group design, no placebo group, small sample size, heterogeneity, statistical significance, potential selection bias, no reporting of complications, no reports of long-term follow up</td>
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<td>Achkar et al. 2010</td>
<td>Systematic review (IV)</td>
<td>14 randomized trials, 431 patients for inclusion</td>
<td>66.2%</td>
<td>LTR 89% (IV)</td>
<td>Prevalence, limited by single-group design, no placebo group, small sample size, heterogeneity, statistical significance, potential selection bias, no reporting of complications, no reports of long-term follow up</td>
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<td>LTR 89% (IV)</td>
<td>Prevalence, limited by single-group design, no placebo group, small sample size, heterogeneity, statistical significance, potential selection bias, no reporting of complications, no reports of long-term follow up</td>
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<td>Guglielmetti et al. 2010</td>
<td>Systematic review (IV)</td>
<td>14 randomized trials, 431 patients for inclusion</td>
<td>66.2%</td>
<td>LTR 89% (IV)</td>
<td>Prevalence, limited by single-group design, no placebo group, small sample size, heterogeneity, statistical significance, potential selection bias, no reporting of complications, no reports of long-term follow up</td>
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<td>Wuorela et al. 2010</td>
<td>Systematic review (IV)</td>
<td>14 randomized trials, 431 patients for inclusion</td>
<td>66.2%</td>
<td>LTR 89% (IV)</td>
<td>Prevalence, limited by single-group design, no placebo group, small sample size, heterogeneity, statistical significance, potential selection bias, no reporting of complications, no reports of long-term follow up</td>
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</table>

RESULTS

Fecal microbiota transplantation is an efficacious, durable, safe and cost-effective treatment for recurrent CDI. Resolution rates reported by the articles ranged from 89 % to 100 % for FMT. The procedure caused resolution without recurrence in long term studies up to 5 years. This durable care is thought to be due to the microbiota change caused by FMT. In addition, the procedure was effective in treating the hypervirulent B1/NAP027 strain. The procedure causes minimal side effects: cramping, belching, nausea, and diarrhea that resolve within 3 h if the inoculum is administered via colonoscopy or nasogastric tube or within 72 h via capsule. A computer analysis conducted by Varela et al was used to predict cost for 90 days of treatment with FMT compared to vancomycin. They determined that FMT was less costly ($1669 vs $3788) and more effective than vancomycin for recurrent CDI. FMT remained superior to vancomycin even when the clinical efficacy was reduced from 94 % to 53 % in the model.

Conclusions

FMT should be considered as first line therapy for RCDI. It is the only therapy to date that uniquely targets the pathophysiologic of CDI and is an effective treatment for hypervirulent C. difficile strains. Despite cost and care benefits, the FDA views it as an investigational procedure. In order to elevate FMT to an FDA approved therapy for CDI, more data needs to be collected. More RCT need to be performed to further prove the effectiveness and safety of FMT for CDI. Available data are based on retrospective case series and include only a single, small size RCT. In addition, RCT should be designed to answer the following questions:

1. What is the optimal protocol for donor-feces infusion: route of administration, volume of inoculum preparation?
2. How should donors be screened and who should be selected for donors?
3. What is the exact impact of FMT on hypervirulent strains?
4. Is it possible to design synthetic stool? What bacterial strains are most effective in restoring a healthy, diverse colonic flora?
5. Should FMT be used after the first recurrence or even as first line treatment?
6. What are the long term adverse effects?

References